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FILE COVERS 1907 - 1 May 2007  VOL 146 ISS 19
FILE LAST UPDATED: 30 Apr 2007  (20070430/ED)

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 substance identification.

=> d que l18
L2              STR
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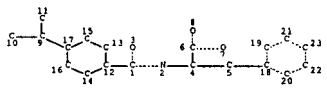

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L15           34 SEA FILE=REGISTRY ABB=ON  PLU=ON  L4 NOT L14
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L17           53 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L12 OR L16
L18           34 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L17 AND L10
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L18  ANSWER 1 OF 34  HCAPLUS  COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:        2005:59980  HCAPLUS  Full-text
DOCUMENT NUMBER:         142:141269
TITLE:                   Crystalline form of nateglinide
INVENTOR(S):             Frenkel, Gustavo; Gome, Boaz; Wizel, Shlomit
PATENT ASSIGNEE(S):      Israel
SOURCE:                  U.S. Pat. Appl. Publ., 91 pp., Cont.-in-part of U.S.
                         Ser. No. 622,905.
                         CODEN: USXXCO
DOCUMENT TYPE:           Patent
LANGUAGE:                English
FAMILY ACC. NUM. COUNT:  4
PATENT INFORMATION:

     PATENT NO.          KIND   DATE        APPLICATION NO.         DATE
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     US 2005014836        A1    20050120    US 2003-746697          20031224
     US 2004181089        A1    20040916    US 2003-622905          20030718 <--
     CA 2513753           A1    20040812    CA 2004-2513753         20040113
     WO 2004067496        A1    20040812    WO 2004-US839           20040113
     WO 2004067496        A9    20041209
         W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
             LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI
     EP 1511717           A1    20050309    EP 2004-701826          20040113
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
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     CN 1835912           A     20060920    CN 2004-80005672        20040113
     US 2007004804        A1    20070104    US 2006-516363          20060905 <--
PRIORITY APPLN. INFO.:                       US 2003-442109P         P  20030123
                                             US 2003-449791P         P  20030224
                                             US 2003-479016P         P  20030616
                                             US 2003-622905          A2 20030718
                                             US 2002-396904P         P  20020718 <--
                                             US 2002-413622P         P  20020925 <--
                                             US 2002-414199P         P  20020926 <--
                                             US 2002-423750P         P  20021105 <--
                                             US 2002-432093P         P  20021210 <--
                                             US 2002-432962P         P  20021212 <--
                                             US 2003-622999          A1 20030718
                                             WO 2003-US22375         A  20030718
                                             US 2003-693166          A  20031023
                                             US 2003-746697          A  20031224
                                             WO 2004-US839           W  20040113

AB   Crystalline forms of nateglinide and processes for their preparation, as well
     as pharmaceutical formulations containing them and methods of administration
     are provided. A process for preparing crystalline form of nateglinide
     comprises the steps of(a) preparing a solution of nateglinide in Et acetate,
     (b) seeding the solution with nateglinide crystals, and (c) recovering the
     crystalline form as a precipitate. The nateglinide obtained is more than about
     99% pure. For example, nateglinide (5 g) was dissolved in acetonitrile,
     acetone, or Et acetate at about 55° in over about 15 min until a clear
     solution was obtained. The solvent was removed to dryness by evaporation at
     about 55°/20 to 30 mmHg to give dry nateglinide crystalline Form B. Also,
     nateglinide Form I was prepared by treating 7.73 g of D-phenylalanine (PheOH)
     with 185 mL (3.5 equiv) of 3.5% NaOH at room temperature to afford a clear
     solution of the corresponding Na-salt. A solution of neat trans-4-
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     isopropylcyclohexanecarboxyl chloride (IPCHAC, 9.02 g, 1.01 equiv) was added
     to the solution of Phe-OH obtained above, over 3 min, while stirring at room
     temperature. The rest of the IPCHAC in the funnel was washed with toluene (1
     mL) and added. The resulting mixture was stirred for 1 h, and was treated
     with 10% HCl (32 mL) to adjust the pH to 3, while stirring. The mixture was
     stirred for 1 h, and filtered. The solid was washed with water (200 mL) and
     sucked well to afford 33.3 g of the moist product, which lost weight after
     drying at 78°/2.2 mbar (Assay 98.4%, purity >99% , yield 86%).
IT   105816-04-4P, Nateglinide
     RL: PEP (Physical, engineering or chemical process); PRP (Properties); PYP
     (Physical process); SPN (Synthetic preparation); THU
     (Therapeutic use); BIOL (Biological study); PREP (Preparation);
     PROC (Process); USES (Uses)
        (preparation of crystalline form of nateglinide for dosage forms)
RN   105816-04-4  HCAPLUS
CN   D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-  (CA
     INDEX NAME)

Absolute stereochemistry.
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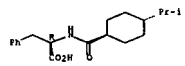

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L18  ANSWER 2 OF 34  HCAPLUS  COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:        2004:203799  HCAPLUS  Full-text
DOCUMENT NUMBER:         140:241062
TITLE:                   Process for the formation of a crystalline polymorphic
                         form of nateglinide
INVENTOR(S):             Reguri, Buchi Reddy; Kadaboina, Rajasekhar;
                         Polavarapu, Srinivas
PATENT ASSIGNEE(S):      Reddy's Laboratories Limited, India; Reddy's
                         Laboratories, Inc.
SOURCE:                  PCT Int. Appl., 29 pp.
                         CODEN: PIXXD2
DOCUMENT TYPE:           Patent
LANGUAGE:                English
FAMILY ACC. NUM. COUNT:  1
PATENT INFORMATION:

     PATENT NO.          KIND   DATE        APPLICATION NO.         DATE
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     WO 2004020396        A1    20040311    WO 2003-US26880         20030827 <--
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             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,
             PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN,
             TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
             KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
             FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
             BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
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     IN 2002MA00631       A     20050304    IN 2002-MA631           20020828 <--
     AU 2003262928        A1    20040319    AU 2003-262928          20030827 <--
     US 2004077725        A1    20040422    US 2003-649380          20030827 <--
PRIORITY APPLN. INFO.:                       IN 2002-MA631        A  20020828 <--
                                             WO 2003-US26880      W  20030827

AB   A crystalline polymorphic form of nateglinide are described and its X-ray
     diffraction pattern presented.
IT   105816-04-4P, Nateglinide
     RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation)
     ; THU (Therapeutic use); BIOL (Biological study); PREP
     (Preparation); RACT (Reactant or reagent); USES (Uses)
       (process for the formation of a crystalline polymorphic form of
nateglinide)
RN   105816-04-4  HCAPLUS
CN   D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-  (CA
     INDEX NAME)

Absolute stereochemistry.
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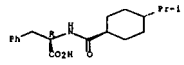

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REFERENCE COUNT:         7     THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS
                               RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18  ANSWER 3 OF 34  HCAPLUS  COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:        2004:203709  HCAPLUS  Full-text
DOCUMENT NUMBER:         140:259085
TITLE:                   Preparation of nateglinide inclusion complexes with
                         cyclodextrins and their use in pharmaceutical
                         compositions
INVENTOR(S):             Niu, Zhanqi; Wang, Lifang; Chen, Yujie; Shen, Dongmin
PATENT ASSIGNEE(S):      Zhongqi Pharmaceutical Technology (Shijiazhuang) Co.,
                         Ltd., Peop. Rep. China
SOURCE:                  PCT Int. Appl., 19 pp.
                         CODEN: PIXXD2
DOCUMENT TYPE:           Patent
LANGUAGE:                Chinese
FAMILY ACC. NUM. COUNT:  1
PATENT INFORMATION:

     PATENT NO.          KIND   DATE        APPLICATION NO.         DATE
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     WO 2004019989        A1    20040311    WO 2003-CN707           20030822 <--
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             HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS,
             LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG,
             PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR,
             TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
             KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
             FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
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BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CN 1478470	A	20040303	CN 2002-132321		20020827 <--
AU 2003255130	A1	20040319	AU 2003-255130		20030822 <--
PRIORITY APPLN. INFO.:			CN 2002-132321	A	20020827 <--
			WO 2003-CN707	W	20030822

AB The invention relates to preparation of inclusion complexes of nateglinide, containing nateglinide and β-cyclodextrin and its derivates, particularly to nateglinide-β-cyclodextrin inclusion complexes. The preparing process comprises saturated solution method, ultrasonic method and grinding method. The inclusion complexes obtained have high stability and can be used in the manufacture of pharmaceutical formulations of nateglinide. For example, nateglinide-β-cyclodextrin (1:2) inclusion complex prepared by grinding the mixture of 10 mL nateglinide (0.0031 mol) ethanol solution and 7g β-cyclodextrin (0.0062 mol), was incorporated into tablets together with starch, crosslinked CMC and magnesium stearate.

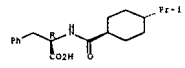
IT ***669087-90-5P***
RL: PRP (Properties); ***SPN (Synthetic preparation)***; THU (Therapeutic use); BIOL (Biological study); ***PREP (Preparation)***; USES (Uses)
(pharmaceutical compns. containing nateglinide inclusion complexes with β-cyclodextrin and its derivs.)

RN 669087-90-5 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-, compd. with β-cyclodextrin (3:1) (9CI) (CA INDEX NAME)

CM 1

CRN 105816-04-4
CMF C19 H27 N O3

Absolute stereochemistry.

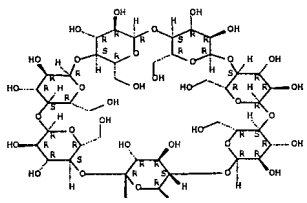


CM 2

CRN 7585-39-9
CMF C42 H70 O35

Absolute stereochemistry.

PAGE 1-A

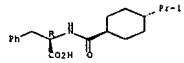


PAGE 2-A

IT ***105816-04-4***, Nateglinide
RL: RCT (Reactant); RACT (Reactant or reagent)
(pharmaceutical compns. containing nateglinide inclusion complexes with β-cyclodextrin and its deriva.)

RN 105816-04-4 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (CA INDEX NAME)

Absolute stereochemistry.

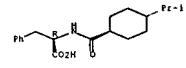


IT ***105816-04-4DP***, Nateglinide, complexes with hydroxypropyl β-cyclodextrin ***669087-91-6P 669087-92-7P 669087-93-8P 669087-94-9P 669087-95-0P 669088-00-0P***
RL: ***SPN (Synthetic preparation)***; THU (Therapeutic use); BIOL (Biological study); ***PREP (Preparation)***; USES (Uses)
(pharmaceutical compns. containing nateglinide inclusion complexes with

β-cyclodextrin and its deriva.)

RN 105816-04-4 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (CA INDEX NAME)

Absolute stereochemistry.

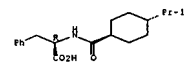


RN 669087-91-6 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-, compd. with β-cyclodextrin (2:1) (9CI) (CA INDEX NAME)

CM 1

CRN 105816-04-4
CMF C19 H27 N O3

Absolute stereochemistry.

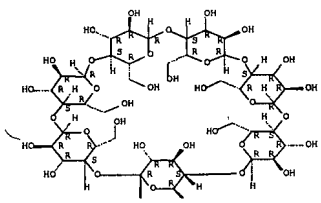


CM 2

CRN 7585-39-9
CMF C42 H70 O35

Absolute stereochemistry.

PAGE 1-A



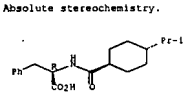
PAGE 2-A

RN 669087-92-7 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-, compd. with 2A,2B,2C,2D,2E,2F,2G,6A,6B,6C,6D,6E,6F,6G-tetradeca-O-methyl-β-cyclodextrin (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 105816-04-4
CMF C19 H27 N O3

Absolute stereochemistry.

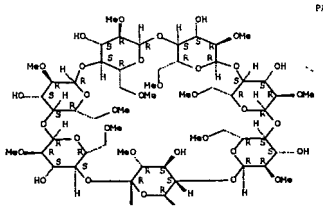


CM 2

CRN 51166-71-3
CMF C56 H98 O35

Absolute stereochemistry.

PAGE 1-A



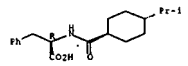
PAGE 2-A

RN 669087-93-8 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-, compd. with 2A,2B,2C,2D,2E,2F,2G,3A,3B,3C,3D,3E,3F,3G,6A,6B,6C,6D,6E,6F,6G-heneicosa-O-methyl-β-cyclodextrin (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 105816-04-4
CMF C19 H27 N O3

Absolute stereochemistry.

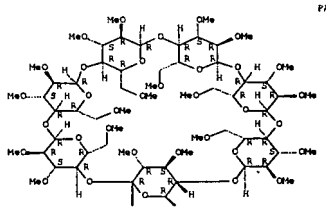


CM 2

CRN 55216-11-0
CMF C63 H112 O35

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A

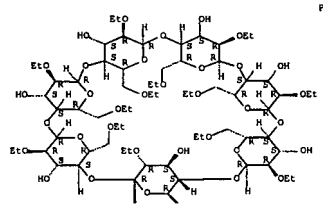
RN 669087-94-9 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-, compd. with 2A,2B,2C,2D,2E,2F,2G,6A,6B,6C,6D,6E,6F,6G-tetradeca-O-ethyl-β-cyclodextrin (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 111689-03-3
CMF C70 H126 O35

Absolute stereochemistry.

PAGE 1-A



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CM 2

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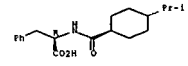
Absolute stereochemistry.

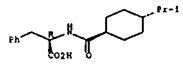


RN 669087-95-0 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-, compd. with β-cyclodextrin (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 105816-04-4
CMF C19 H27 N O3

Absolute stereochemistry.



CM 2

CRN 7585-39-9
CMF C42 H70 O35

Absolute stereochemistry.

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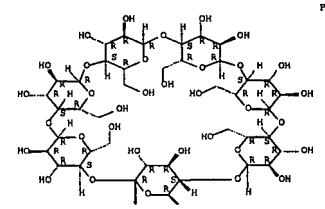


PAGE 2-A

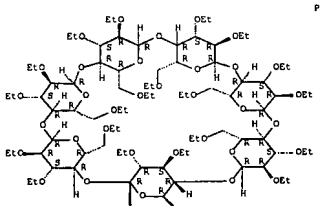
RN 669088-00-0 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-, compd. with 2A,2B,2C,2D,2E,2F,2G,3A,3B,3C,3D,3E,3F,3G,6A,6B,6C,6D,6E,6F,6G-heneicosa-O-ethyl-β-cyclodextrin (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 111689-01-1
CMF C84 H154 O35

Absolute stereochemistry.

PAGE 1-A

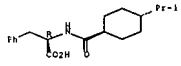


PAGE 2-A

CM 2

CRN 105816-04-4
CMF C19 H27 N O3

Absolute stereochemistry.



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 4 OF 34 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:162826 HCAPLUS Full-text
DOCUMENT NUMBER: 140:199745
TITLE: Synthesis and purification of nateglinide
INVENTOR(S): Naik, Samir Jaivant; Kulkarni, Pramila Vijay; Gaikwad, Nandkumar Baburao; Sawant, Mangesh Shivram; Bhirud, Shekhar; Batchu, Chandrasekhar
PATENT ASSIGNEE(S): Glenmark Pharmaceuticals Limited, India
SOURCE: PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004018408	A1	20040304	WO 2003-IB3270	20030812 <--
WO 2004018408	A8	20050310		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
IN 2002MU00773	A	20040605	IN 2002-MU773	20020826 <--
AU 2003263386	A1	20040311	AU 2003-263386	20030812 <--
PRIORITY APPLN. INFO.:			IN 2002-MU773	A 20020826 <--
			WO 2003-IB3270	W 20030812

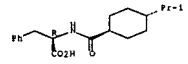
OTHER SOURCE(S): CASREACT 140:199745; MARPAT 140:199745

AB N-[(trans-4-isopropylcyclohexyl)carbonyl]-D-phenylalanine (nateglinide) was prepared by reaction of trans-4-isopropylcyclohexylcarboxylic acid with an alkyl chloroformate in a ketonic solvent in the presence of a base at -20 to 30°C and reaction of the mixed anhydride product with an aqueous alkali salt solution of D-phenylalanine. An example shows the synthesis of nateglinide by using triethylamine and Et chloroformate in acetone (97% pure following HPLC).

IT ***105816-04-4P***, Nateglinide
RL: ***IMF (Industrial manufacture); PUR (Purification or recovery); SPN (Synthetic preparation); PREP (Preparation)***
(synthesis and purification of nateglinide)

RN 105816-04-4 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 5 OF 34 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:80637 HCAPLUS Full-text
DOCUMENT NUMBER: 140:151932
TITLE: Preparation of polymorphic forms of nateglinide
INVENTOR(S): Yahalomi, Ronit; Shapior, Evgeny; Dolitzky, Ben-zion; Gozlan, Yigael; Gome, Boaz
PATENT ASSIGNEE(S): Teva Pharmaceutical Industries Ltd., Israel; Teva Pharmaceutical Usa, Inc.
SOURCE: PCT Int. Appl., 130 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004009532	A1	20040129	WO 2003-US22375	20030718 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004152782	A1	20040805	US 2003-614266	20030703 <--
US 6861553	B2	20050301		
CA 2492644	A1	20040129	CA 2003-2492644	20030718 <--
AU 2003253971	A1	20040209	AU 2003-253971	20030718 <--
US 2004116526	A1	20040617	US 2003-623237	20030718 <--
US 7148376	B2	20061212		
EP 1467964	A1	20041020	EP 2003-765665	20030718 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
US 2005014949	A1	20050120	US 2003-623290	20030718 <--
US 2005075400	A1	20050407	US 2003-622999	20030718 <--
CN 1723180	A	20060118	CN 2003-821921	20030718 <--
JP 2006511614	T	20060406	JP 2005-505521	20030718 <--
CA 2513753	A1	20040812	CA 2004-2513753	20040113
WO 2004067496	A1	20040812	WO 2004-US839	20040113
WO 2004067496	A9	20041209		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI				
EP 1511717	A1	20050309	EP 2004-701826	20040113
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
CN 1835912	A	20060920	CN 2004-80005672	20040113
US 2007004804	A1	20070104	US 2006-516363	20060905 <--
PRIORITY APPLN. INFO.:			US 2002-396904P	P 20020718 <--
			US 2002-413622P	P 20020925 <--
			US 2002-414199P	P 20020926 <--
			US 2002-423750P	P 20021105 <--

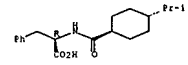
US 2002-432093P	P	20021210 <--	
US 2002-432962P	P	20021212 <--	
US 2003-442109P	P	20030123	
US 2003-449791P	P	20030224	
US 2003-479016P	P	20030616	
US 2003-614266	A	20030703	
US 2002-393495P	P	20020703 <--	
US 2003-622905	A	20030718	
US 2003-622999	A1	20030718	
WO 2003-US22375	W	20030718	
US 2003-693166	A	20031023	
US 2003-746697	A	20031224	
WO 2004-US839	W	20040113	

AB The invention discloses the preparation of 26 characterized forms of nateglinide (forms A, C, D, F, G, I, J, K, L, M, N, O, P, Q, T, U, V, Y, α, β, γ, δ, ε, σ, θ and Ω). Most of the forms are solvates (with the exception of forms L, P, U, α, δ and σ). Polymorphic forms are characterized by their mp, DSC, XRPD, FTIR; form interconversion is also discussed. For example, D-phenylalanine is reacted with trans-[(4- (isopropyl)cyclohexane]carbonyl]chloride (i. NaOH&q; ii. H2SO4). The wet cake of nateglinide is dissolved in EtOAc, the aqueous phase is removed and the resulting solution heated to 50° under reduced pressure and added to hot heptane. The resulting solution is cooled and seeded with the B-form to afford the δ-form (33% yield).

IT ***105816-04-4P***, Nateglinide
RL: PEP (Physical, engineering or chemical process); PYP (Physical process); RCT (Reactant); ***SPN (Synthetic preparation)***; THU (Therapeutic use); BIOL (Biological study); ***PREP (Preparation)***; PROC (Process); RACT (Reactant or reagent); USES (Uses)
(preparation of polymorphic forms of nateglinide)

RN 105816-04-4 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (CA INDEX NAME)

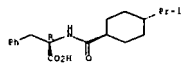
Absolute stereochemistry.



IT ***105816-04-4DP***, Nateglinide, polymorphs ***651353-42-3P 651353-43-4P 651353-44-5P 651353-45-6P 651353-46-7P 651353-47-8P 651353-48-9P 651353-49-0P 651353-50-3P 651353-51-4P 651353-52-5P 651353-53-6P 651353-54-7P***
RL: PEP (Physical, engineering or chemical process); PYP (Physical process); ***SPN (Synthetic preparation)***; THU (Therapeutic use); BIOL (Biological study); ***PREP (Preparation)***; PROC (Process); USES (Uses)
(preparation of polymorphic forms of nateglinide)

RN 105816-04-4 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (CA INDEX NAME)

Absolute stereochemistry.

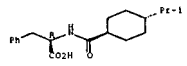


RN 651353-42-3 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-, compd. with methanol (9CI) (CA INDEX NAME)

CM 1

CRN 105816-04-4
CMF C19 H27 N O3

Absolute stereochemistry.



CM 2

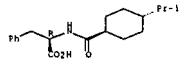
CRN 67-56-1
CMF C H4 O

RN 651353-43-4 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-, compd. with ethanol (9CI) (CA INDEX NAME)

CM 1

CRN 105816-04-4
CMF C19 H27 N O3

Absolute stereochemistry.



CM 2

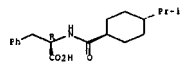
CRN 64-17-5
CMF C2 H6 O

RN 651353-44-5 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-, compd. with 1-butanol (9CI) (CA INDEX NAME)

CM 1

CRN 105816-04-4
CMF C19 H27 N O3

Absolute stereochemistry.



CM 2

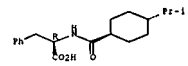
CRN 71-36-3
CMF C4 H10 O

RN 651353-45-6 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-, compd. with 1-propanol (9CI) (CA INDEX NAME)

CM 1

CRN 105816-04-4
CMF C19 H27 N O3

Absolute stereochemistry.



CM 2

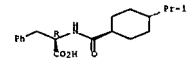
CRN 71-23-8
CMF C3 H8 O

RN 651353-46-7 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-, compd. with N,N-dimethylacetamide (9CI) (CA INDEX NAME)

CM 1

CRN 105816-04-4
CMF C19 H27 N O3

Absolute stereochemistry.



CM 2

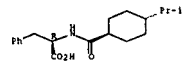
CRN 127-19-5
CMF C4 H9 N O

RN 651353-47-8 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-, compd. with 1-methyl-2-pyrrolidinone (9CI) (CA INDEX NAME)

CM 1

CRN 105816-04-4
CMF C19 H27 N O3

Absolute stereochemistry.



CM 2

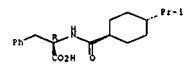
CRN 872-50-4
CMF C5 H9 N O

RN 651353-48-9 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-, compd. with N,N-dimethylformamide (9CI) (CA INDEX NAME)

CM 1

CRN 105816-04-4
CMF C19 H27 N O3

Absolute stereochemistry.



CM 2

CRN 68-12-2

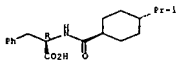
CMF C3 H7 N O

RN 651353-49-0 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-, compd. with 1,2-dimethoxyethane (9CI) (CA INDEX NAME)

CM 1

CRN 105816-04-4
CMF C19 H27 N O3

Absolute stereochemistry.



CM 2

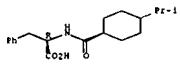
CRN 110-71-4
CMF C4 H10 O2

RN 651353-50-3 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-, compd. with dimethylbenzene (9CI) (CA INDEX NAME)

CM 1

CRN 105816-04-4
CMF C19 H27 N O3

Absolute stereochemistry.



CM 2

CRN 1330-20-7
CMF C8 H10
CCI IDS

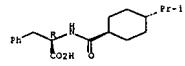
2 (D1-Me)

RN 651353-51-4 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-, compd. with tetrachloromethane (9CI) (CA INDEX NAME)

CM 1

CRN 105816-04-4
CMF C19 H27 N O3

Absolute stereochemistry.



CM 2

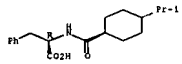
CRN 56-23-5
CMF C Cl4

RN 651353-52-5 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-, compd. with 1,2-dichloroethane (9CI) (CA INDEX NAME)

CM 1

CRN 105816-04-4
CMF C19 H27 N O3

Absolute stereochemistry.



CM 2

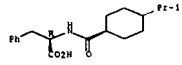
CRN 107-06-2
CMF C2 H4 Cl2

RN 651353-53-6 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-, compd. with trichloromethane (9CI) (CA INDEX NAME)

CM 1

CRN 105816-04-4
CMF C19 H27 N O3

Absolute stereochemistry.



CM 2

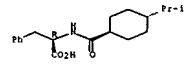
CRN 67-66-3
CMF C H Cl3

RN 651353-54-7 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-, compd. with heptane (9CI) (CA INDEX NAME)

CM 1

CRN 105816-04-4
CMF C19 H27 N O3

Absolute stereochemistry.



CM 2

CRN 142-82-5
CMF C7 H16

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 6 OF 34 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:41431 HCAPLUS Full-text
DOCUMENT NUMBER: 140:94292
TITLE: Process for preparing nateglinide and its intermediates
INVENTOR(S): Yahalomi, Ronit; Shapiro, Evgeny; Dolitzky, Ben-zion; Gozlan, Yigael
PATENT ASSIGNEE(S): Teva Pharmaceutical Industries Ltd., Israel; Teva Pharmaceuticals Usa, Inc.
SOURCE: PCT Int. Appl., 31 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004005240	A1	20040115	WO 2003-US21238	20030703 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,				

LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,
PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN,
TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2003256454	A1	20040123	AU 2003-256454	20030703	<--
EP 1487782	A1	20041222	EP 2003-763310	20030703	<--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK					
CN 1671649	A	20050921	CN 2003-817439	20030703	<--
US 2004116526	A1	20040617	US 2003-623237	20030718	<--
US 7148376	B2	20061212			
US 2005014949	A1	20050120	US 2003-623290	20030718	<--
US 2005075400	A1	20050407	US 2003-622999	20030718	<--
CN 1723190	A	20060118	CN 2003-821921	20030718	<--
US 2007004804	A1	20070104	US 2006-516363	20060905	<--

PRIORITY APPLN. INFO.:

US 2002-393495P	P	20020703 <--
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US 2002-414199P	P	20020926 <--
US 2002-423750P	P	20021105 <--
US 2002-432093P	P	20021210 <--
US 2002-432962P	P	20021212 <--
US 2003-442109P	P	20030123
US 2003-449791P	P	20030224
US 2003-479016P	P	20030616
WO 2003-US21238	W	20030703
US 2003-622999	A1	20030718

OTHER SOURCE(S): CASREACT 140:94292

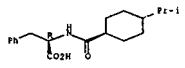
AB A process for the preparation of nateglinide involves converting trans-4-isopropylcyclohexanecarboxylic acid into the acid chloride by reaction with thionyl chloride in the presence of an organic amide and acylation of a suitable salt of D-phenylalanine with the acid chloride in a single or two phase system or in water free of a co-solvent.

IT ***105816-04-4P***, Nateglinide
RL: ***IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)***
(process for preparation of nateglinide)

RN 105816-04-4 HCAPLUS

CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (CA INDEX NAME)

Absolute stereochemistry.

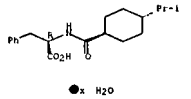


IT ***173653-89-9***
RL: PRP (Properties)
(properties of nateglinide hydrate)

RN 173653-89-9 HCAPLUS

CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-, hydrate (9CI) (CA INDEX NAME)

Absolute stereochemistry.



●x H2O

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 7 OF 34 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:892741 HCAPLUS Full-text
DOCUMENT NUMBER: 139:369757
TITLE: Process for the preparation of a crystal polymorphic form of N-(trans-4-isopropylcyclohexylcarbonyl)-D-phenylalanine (nateglinide)
INVENTOR(S): Rajamahendra, Shanmughasamy; Aswathanarayanappa, Chandrashekar; Puthiaparampil, Tom Thomas; Sridharan, Madhavan; Ganesh, Sambasivam
PATENT ASSIGNEE(S): Biocon India Limited, India
SOURCE: PCT Int. Appl., 19 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
WO 2003093222	A1	20031113	WO 2002-IN114	20020429	<--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
CA 2481322	A1	20031113	CA 2002-2481322	20020429	<--
AU 2002304281	A1	20031117	AU 2002-304281	20020429	<--
EP 1499586	A1	20050126	EP 2002-733208	20020429	<--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
HU 2005000259	A2	20050628	HU 2005-259	20020429	<--
US 2005165108	A1	20050728	US 2003-508364	20020429	<--
JP 2005523933	T	20050811	JP 2004-501362	20020429	<--

PRIORITY APPLN. INFO.:

WO 2002-IN114	W	20020429 <--

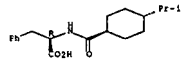
AB Novel polymorph Form C of N-(trans-4-isopropylcyclohexylcarbonyl)-D-phenylalanine (I; i.e., nateglinide) is produced having a different IR spectrum and X-ray diffraction patterns (presented) from previously known forms of I.

IT ***105816-04-4P***, Nateglinide
RL: ***IMF (Industrial manufacture)***; PEP (Physical, engineering or chemical process); PRP (Properties); PYP (Physical process); ***PREP (Preparation)***; PROC (Process)
(process for the preparation of a crystal polymorphic form of N-(trans-4-isopropylcyclohexylcarbonyl)-D-phenylalanine (nateglinide))

RN 105816-04-4 HCAPLUS

CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 8 OF 34 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:837030 HCAPLUS Full-text
DOCUMENT NUMBER: 139:341723
TITLE: Novel nateglinide crystals
INVENTOR(S): Koguchi, Yoshihito; Nakao, Tomoko; Sumikawa, Michito
PATENT ASSIGNEE(S): Ajinomoto Co., Inc., Japan
SOURCE: PCT Int. Appl., 17 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
WO 2003087039	A1	20031023	WO 2003-JP4686	20030414	<--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
AU 2003236243	A1	20031027	AU 2003-236243	20030414	<--
EP 1496048	A1	20050112	EP 2003-746474	20030414	<--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK					
US 2005101672	A1	20050512	US 2004-965171	20041015	<--

PRIORITY APPLN. INFO.:

JP 2002-111963	A	20020415 <--
WO 2003-JP4686	W	20030414

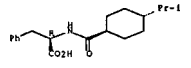
AB A type crystal (powder X-ray diffraction main peaks: 4.4°, 5.2°, 15.7°, 18.5° (2 theta)), M type crystal (powder X-ray diffraction main peaks: 6.0°, 14.2°, 15.2°, 18.8° (2 theta)), and P type crystal (powder X-ray diffraction main peaks: 4.8°, 5.3°, 14.3°, 15.2° (2 theta)) of nateglinide, which are all novel crystals, can be prepared by a method comprising dissolving nateglinide in a solvent exhibiting high solubility for nateglinide and then adding a solvent exhibiting poor solubility for nateglinide or dissolving nateglinide in a mixed solvent comprising a solvent exhibiting high solubility for nateglinide and a solvent exhibiting poor solubility for nateglinide and then cooling the resulting nateglinide solution to precipitate crystals, subjecting the product to filtration, and then drying at a specific temperature Nateglinide is a known antidiabetic.

IT ***105816-04-4P***, Nateglinide
RL: PRP (Properties); ***PUR (Purification or recovery)***; THU (Therapeutic use); BIOL (Biological study); ***PREP (Preparation)***; USES (Uses)
(preparation of A, H, and P type nateglinide crystals by crystallization from mixture of solvents)

RN 105816-04-4 HCAPLUS

CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 9 OF 34 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:737716 HCAPLUS Full-text
DOCUMENT NUMBER: 139:230996
TITLE: Preparation and properties of nateglinide salts
INVENTOR(S): Sutton, Paul Allen; Vivilecchia, Richard Victor; Parker, David John; De La Cruz, Marilyn
PATENT ASSIGNEE(S): Novartis Ag, Switz.; Novartis Pharma Gmbh
SOURCE: PCT Int. Appl., 46 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
WO 2003076393	A1	20030918	WO 2003-EP2447	20030310	<--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LT, LU,					

LV, MA, MD, MK, MN, MX, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SE, SG, SK, TJ, TM, TN, TR, TT, UA, US, UZ, VC, VN, YU, ZA, ZW
RW: AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR

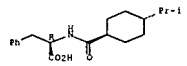
CA 2478599	A1	20030918	CA 2003-2478599		20030310 <--
AU 2003214112	A1	20030922	AU 2003-214112		20030310 <--
EP 1483232	A1	20041208	EP 2003-709769		20030310 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK					
BR 2003008316	A	20041228	BR 2003-8316		20030310 <--
JP 2005519949	T	20050707	JP 2003-574615		20030310 <--
CN 1642904	A	20050720	CN 2003-805803		20030310 <--
US 2005234129	A1	20051020	US 2004-507255		20040928 <--
PRIORITY APPLN. INFO.:			US 2002-363178P	P	20020311 <--
			WO 2003-EP2447	W	20030310

AB The invention relates to salts of nateglinide having specified properties (m.ps., solubilities, X-ray diffraction patterns) for use in pharmaceutical compns. for preventing or treating diabetes, cardiovascular diseases, etc. Nateglinide Na, K, Ca, Mg, N-methyl-D-glucamine, TRIS, lysine, and ammonium salts were prepared and their properties tabulated.

IT ***105816-04-4***, Nateglinide
RL: PRP (Properties); RCT (Reactant); RACT (Reactant or reagent)
(preparation and properties of nateglinide salts)

RN 105816-04-4 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (CA INDEX NAME)

Absolute stereochemistry.



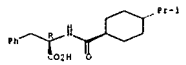
IT ***592523-31-4P 592523-32-5P 592524-24-8P 594837-85-1P 594837-86-2P 594837-87-3P 594837-89-5P***
RL: PRP (Properties); ***SPN (Synthetic preparation); PREP (Preparation)***
(preparation and properties of nateglinide salts)

RN 592523-31-4 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-, compd. with 1-deoxy-1-(methylamino)-D-glucitol (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 105816-04-4
CMF C19 H27 N O3

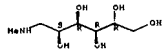
Absolute stereochemistry.



CM 2

CRN 6284-40-8
CMF C7 H17 N O5

Absolute stereochemistry.

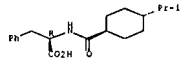


RN 592523-32-5 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-, compd. with 2-amino-2-(hydroxymethyl)-1,3-propanediol (1:1) (9CI) (CA INDEX NAME)

CM 1

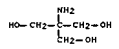
CRN 105816-04-4
CMF C19 H27 N O3

Absolute stereochemistry.



CM 2

CRN 77-86-1
CMF C4 H11 N O3

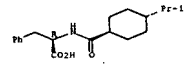


RN 592524-24-8 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-, compd. with L-lysine (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 105816-04-4
CMF C19 H27 N O3

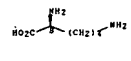
Absolute stereochemistry.



CM 2

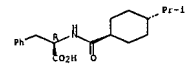
CRN 56-87-1
CMF C6 H14 N2 O2

Absolute stereochemistry.



RN 594837-85-1 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-, monosodium salt (9CI) (CA INDEX NAME)

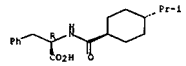
Absolute stereochemistry.



● Na

RN 594837-86-2 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-, monopotassium salt (9CI) (CA INDEX NAME)

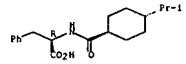
Absolute stereochemistry.



● K

RN 594837-87-3 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-, calcium salt (2:1) (9CI) (CA INDEX NAME)

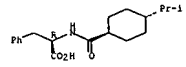
Absolute stereochemistry.



● 1/2 Ca

RN 594837-89-5 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-, ammonium salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● x NH3

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

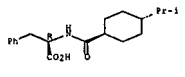
L18 ANSWER 10 OF 34 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:76738 HCAPLUS Full-text
DOCUMENT NUMBER: 138:137033
TITLE: Oxidative process and catalysts for the manufacture of

para-substituted benzoic acids from their corresponding aldehydes
INVENTOR(S): Girgis, Michael John; Shekhar, Ratna
PATENT ASSIGNEE(S): Novartis AG, Switz.
SOURCE: PCT Int. Appl., 15 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003008367	A2	20030130	WO 2002-US22631	20020716 <--
WO 2003008367	A3	20030410		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003023115	A1	20030130	US 2002-196600	20020715 <--
US 6740776	B2	20040525		
AU 2002313681	A1	20030303	AU 2002-313681	20020716 <--
PRIORITY APPLN. INFO.:			US 2001-305648P P	20010716 <--
			WO 2002-US22631 W	20020716 <--

OTHER SOURCE(S): CASREACT 138:137033; MARPAT 138:137033
AB A low-temperature process for preparing aromatic acids 4-(R1R2CH)C6H4CO2H [R1, R2 = H, C1-8 (un)branched alkyl, cycloalkyl; e.g., 4-isopropylbenzoic acid] comprises oxidizing the corresponding aromatic aldehyde 4-(R1R2CH)C6H4CHO (e.g., 4-isopropylbenzaldehyde) with a gas having an oxygen content of 1-100% at 20° to <100° in the presence of a supported Group VIII metal catalyst (e.g., Pt/C), and using a solvent having a flash point >95°C and/or a m.p. <55°, provided that the flash point of the solvent is greater than the reaction temperature
IT ***105816-04-4P***, Nateglinide
RL: ***PNU (Preparation, unclassified); PREP (Preparation)***
(preparation of)
RN 105816-04-4 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (CA INDEX NAME)

Absolute stereochemistry.



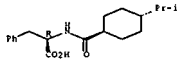
L18 ANSWER 11 OF 34 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2003:62632 HCAPLUS Full-text
DOCUMENT NUMBER: 138:73015
TITLE: Synthesis process for trans-4-isopropylcyclohexanecarboxylic acid
INVENTOR(S): Gu, Lianquan; An, Linkun; Ma, Lin; Guo, Xindong; Huang, Zhizhu
PATENT ASSIGNEE(S): Zhongshan Univ., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 6 pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1319583	A	20011031	CN 2001-107459	20010116 <--
PRIORITY APPLN. INFO.:			CN 2001-107459	20010116 <--

OTHER SOURCE(S): CASREACT 138:73015
AB The process comprises hydrogenating cumic acid in acetic acid in the presence of PtO2, recovering solvent, treating with 10-25% inorg. base (such as Ba(OH)2, Mg(OH)2, KOH, or NaOH) solution at 50-150° for 10-20 h, neutralizing with HCl to pH 2, crystallizing, filtering, and recrystg. in methanol.
IT ***105816-04-4P***, Nateglinide
RL: ***PNU (Preparation, unclassified); PREP (Preparation)***
(synthesis of trans-4-isopropylcyclohexanecarboxylic acid as intermediate for nateglinide)
RN 105816-04-4 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (CA INDEX NAME)

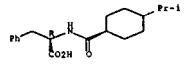
Absolute stereochemistry.



L18 ANSWER 12 OF 34 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:30017 HCAPLUS Full-text
DOCUMENT NUMBER: 139:210299
TITLE: Study on separation of cis-isomer of nateglinide by high-pressure liquid chromatographic method
AUTHOR(S): Yan, Xiaoyan; Hu, Xin; Cao, Guoying; He, Xiaorong; Yin, Qi
CORPORATE SOURCE: Beijing Hospital, Ministry of Public Health, Beijing, 100730, Peop. Rep. China
SOURCE: Zhongguo Yaoxue Zazhi (Beijing, China) (***2002***), 37(6), 444-446
CODEN: ZYZAEU; ISSN: 1001-2494
PUBLISHER: Zhongguo Yaoxue Zazhishe
DOCUMENT TYPE: Journal
LANGUAGE: Chinese

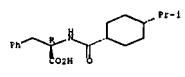
AB A high-pressure liquid chromatog. method for the separation of cis-isomer of nateglinide was established on Phenomenex Luna C18 column (5 μm, 4.6 mm x 250 mm) with UV detection at 214 nm and room temperature The mobile phase was consisted of (A) acetonitrile and (B) 0.03 mol L-1 phosphate buffer (pH 2.5, 65:35, volume/volume). The resolution factors were at least 1.5. The limits of detection and quantitation limit was 0.06 and 0.18 μg mL-1, resp. The method is useful in separation and determination of the cis-isomer from nateglinide.
IT ***105816-04-4P 105816-06-6P***
RL: ANT (Analyte); BSU (Biological study, unclassified); PRP (Properties); ***PUR (Purification or recovery)***; ANST (Analytical study); BIOL (Biological study); ***PREP (Preparation)***
(separation of cis-isomer of nateglinide by HPLC method)
RN 105816-04-4 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (CA INDEX NAME)

Absolute stereochemistry.



RN 105816-06-6 HCAPLUS
CN D-Phenylalanine, N-[[cis-4-(1-methylethyl)cyclohexyl]carbonyl]- (9CI) (CA INDEX NAME)

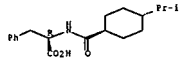
Absolute stereochemistry.



L18 ANSWER 13 OF 34 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:8839 HCAPLUS Full-text
DOCUMENT NUMBER: 139:270189
TITLE: Pharmacokinetics of nateglinide and its racemization during biotransformation in healthy volunteers
AUTHOR(S): Hu, Xin; Cao, Guoying; Wu, Xiuzhong; Song, Youhua; Sun, Chunhua
CORPORATE SOURCE: Department of Pharmacy, Beijing Hospital, Beijing, 100730, Peop. Rep. China
SOURCE: Zhongguo Linchuang Yaolixue Zazhi (***2003***), 18(3), 195-199
CODEN: ZLYZE9; ISSN: 1001-6821
PUBLISHER: Beijing Yike Daxue, Linchuang Yaoli Yanjiuso
DOCUMENT TYPE: Journal
LANGUAGE: Chinese

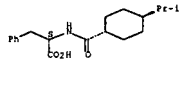
AB The pharmacokinetics of nateglinide and its racemization during biotransformation were studied in 8 healthy volunteers. Each volunteer was orally given 90 mg. Drug concns. in plasma and urine were assayed by RP-HPLC method on Chiralcel ODR column (10 μm, 4.6 mm x 250 mm) with acetonitrile-0.5 mol L-1 sodium perchlorate (70:30, pH 2.2) as mobile phase with detection at 214 nm. Pharmacokinetic parameters were calculated on the basis of non-compartment model. After a single oral dose (90 mg), Cmax was 7.51 ± 2.83 mg L-1 at 1.25 ± 0.26 h, t1/2 was 1.18 ± 0.33 h, AUC0-i was 17.97 ± 4.34 mg h-1 L-1, CL/F (s) was 5.30 ± 1.46 L h-1, original drug percentage in urine within 12 h was 6.23% ± 0.86%. The L-enantiomer could not be detected in either plasma or urine. Nateglinide had a rapid absorption and exclusion. The racemization of D-enantiomer in vivo was not observed
IT ***105816-04-4***, Nateglinide ***105816-05-5***, L-Nateglinide
RL: PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmacokinetics of nateglinide and its racemization during biotransformation in healthy volunteers)
RN 105816-04-4 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (CA INDEX NAME)

Absolute stereochemistry.



RN 105816-05-5 HCAPLUS
CN L-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (9CI) (CA INDEX NAME)

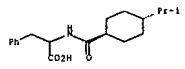
Absolute stereochemistry.



L18 ANSWER 14 OF 34 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:864977 HCAPLUS Full-text
DOCUMENT NUMBER: 138:146886
TITLE: Chiral separation of N-(trans-4-isopropylcyclohexylcarbonyl)-D,L-phenylalanine isomers by high performance liquid chromatography
AUTHOR(S): Yang, Gengliang; Li, Zhiwei; Wang, Dexian; Zhang, Zhefeng; Liu, Erdong; Chen, Yi
CORPORATE SOURCE: College of Chemistry and Environmental Science, Hebei University, Baoding, 071002, Peop. Rep. China
SOURCE: Chromatographia (***2002***), 56(7/8), 515-518

CODEN: CHGBH7; ISSN: 0009-5893
PUBLISHER: Friedrich Vieweg & Sohn Verlagsgesellschaft mbH
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A HPLC method was developed for the chiral separation of a new anti-diabetic agent, N-(trans-4-isopropylcyclohexylcarbonyl)-D-phenylalanine, and its L-enantiomer. The separation was performed on a Sumichiral OA-3200 column. Optimized mobile phase was 0.025 mol L-1 ammonium acetate in methanol solution UV detection was at 210 nm. Baseline chiral separation was obtained within 12 min. The detection limits are 80 pg for the D-enantiomer and 120 pg for the L-enantiomer. Relative standard deviation of the method was <1% (n = 5).
IT ***491828-09-2***
RL: ANT (Analyte); ANST (Analytical study)
(chiral separation of N-(trans-isopropylcyclohexylcarbonyl)-DL-phenylalanine
isomers by high performance liquid chromatog.)
RN 491828-09-2 HCAPLUS
CN Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (9CI) (CA INDEX NAME)

Relative stereochemistry.

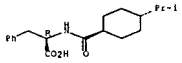


REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 15 OF 34 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:609152 HCAPLUS Full-text
DOCUMENT NUMBER: 138:254901
TITLE: a new synthesis method of nateglinide as antidiabetic drug
AUTHOR(S): Wang, Dun; Liang, Yiheng; Gong, Ping; Zhao, Yanfang
CORPORATE SOURCE: School of Pharmaceutical Engineering, Shenyang Pharmaceutical University, Shenyang, 110016, Peop. Rep. China
SOURCE: Zhongguo Yaowu Huaxue Zazhi (***2002***), 12(2), 94-96
CODEN: ZYHZEF; ISSN: 1005-0108
PUBLISHER: Zhongguo Yaowu Huaxue Zazhi Bianjibu
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
OTHER SOURCE(S): CASREACT 138:254901
AB A new antidiabetic drug-nateglinide was synthesized from isopropylbenzene by Friedel-Crafts reaction, chloroform reaction, catalytic hydrogenation to obtain trans-4-isopropylhexanecarboxylic acid, acylation of D-phenylalanine Et ester, hydrolysis to obtain nateglinide B-type crystal, and crystal-conversion. The total yield was 9.8%.
IT ***105816-04-4P***, Nateglinide
RL: ***SPN (Synthetic preparation)***; THU (Therapeutic use); BIOL (Biological study); ***PREP (Preparation)***; USES (Uses)
(synthesis of nateglinide as antidiabetic drug)

RN 105816-04-4 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (CA INDEX NAME)

Absolute stereochemistry.



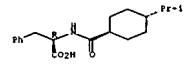
L18 ANSWER 16 OF 34 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:332157 HCAPLUS Full-text
DOCUMENT NUMBER: 136:340998
TITLE: Process for producing B-form nateglinide crystals
INVENTOR(S): Sumikawa, Michito; Maruo, Makoto; Miyazaki, Kazuo; Nishina, Shigehiro; Matsuzawa, Yukiko
PATENT ASSIGNEE(S): Ajinomoto Co., Inc., Japan
SOURCE: PCT Int. Appl., 9 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2002034713	A1	20020502	WO 2001-JP9293		20011023 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
AU 200196001	A	20020506	AU 2001-96001		20011023 <--
CA 2426745	A1	20030423	CA 2001-2426745		20011023 <--
EP 1334964	A1	20030813	EP 2001-976819		20011023 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
BR 2001014846	A	20040225	BR 2001-14846		20011023 <--
RU 2275354	C2	20060427	RU 2003-111948		20011023 <--
US 2003229249	A1	20031211	US 2003-421888		20030424 <--
IN 2003CN00609	A	20050415	IN 2003-CN609		20030424 <--
PRIORITY APPLN. INFO.:			JP 2000-324375	A	20001024 <--
			WO 2001-JP9293	W	20011023 <--

AB A process for producing B-form nateglinide crystals containing substantially no H-form crystals comprises the steps of drying wet crystals of a nateglinide solvate at a low temperature until the solvent disappears and then causing them to undergo a crystal transition. Nateglinide is a known antidiabetic. By this process, B-form nateglinide crystals can be produced on an industrial scale.

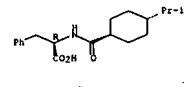
IT ***105816-04-4P***, Nateglinide
RL: PAC (Pharmacological activity); ***PUR (Purification or recovery)***; THU (Therapeutic use); BIOL (Biological study); ***PREP (Preparation)***; USES (Uses)
(industrial process for producing B-form nateglinide crystals)
RN 105816-04-4 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (CA INDEX NAME)

Absolute stereochemistry.



IT ***173653-89-9***
RL: PEP (Physical, engineering or chemical process); PROC (Process)
(industrial process for producing B-form nateglinide crystals)
RN 173653-89-9 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-, hydrate (9CI) (CA INDEX NAME)

Absolute stereochemistry.



x H2O

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

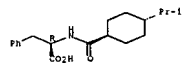
L18 ANSWER 17 OF 34 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:314896 HCAPLUS Full-text
DOCUMENT NUMBER: 136:325825
TITLE: Process for producing nateglinide crystals
INVENTOR(S): Takahashi, Daisuke; Nishi, Seiichi; Takahashi, Satoji
PATENT ASSIGNEE(S): Ajinomoto Co., Inc., Japan
SOURCE: PCT Int. Appl., 14 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2002032854	A1	20020425	WO 2001-JP9069	20011016 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2001094265	A	20020429	AU 2001-94265	20011016 <--
CA 2425538	A1	20030410	CA 2001-2425538	20011016 <--
EP 1334963	A1	20030813	EP 2001-974875	20011016 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2001014729	A	20031014	BR 2001-14729	20011016 <--
RU 2273629	C2	20060410	RU 2003-111021	20011016 <--
CN 1769263	A	20060510	CN 2005-10118852	20011016 <--
TW 251588	B	20060321	TW 2001-90125697	20011017 <--
IN 2003CN00537	A	20050415	IN 2003-CN537	20030411 <--
US 2004030182	A1	20040212	US 2003-418105	20030418 <--
US 7208622	B2	20070424		
PRIORITY APPLN. INFO.:			JP 2000-317604	A 20001018 <--
			CN 2001-820658	A3 20011016 <--
			WO 2001-JP9069	W 20011016 <--

OTHER SOURCE(S): CASREACT 136:325825
AB A process for producing nateglinide crystals comprises reacting trans-4-isopropylcyclohexylcarbonyl chloride with D-phenylalanine in a mixed solvent consisting of a ketone solvent and water in the presence of an alkali to obtain a reaction mixture containing nateglinide, adding an acid to the reaction mixture to make it acidic, and regulating (a) the temperature to 58° to 72° and (b) and the ketone solvent concentration to > 8 weight% and < 22 weight%, to conduct crystallization Nateglinide is a known antidiabetic. The process is an industrially advantageous method for crystallizing nateglinide.
IT ***105816-04-4P***, Nateglinide
RL: ***IMF (Industrial manufacture)***; PRP (Properties); ***PUR (Purification or recovery)***; ***SPN (Synthetic preparation)***; THU (Therapeutic use); BIOL (Biological study); ***PREP (Preparation)***; USES (Uses)
(process for producing nateglinide crystals)
RN 105816-04-4 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 18 OF 34 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2002:314895 HCAPLUS Full-text
DOCUMENT NUMBER: 136:340997
TITLE: Process for preparation of acylphenylalanines
INVENTOR(S): Sumikawa, Michito; Ohgane, Takao
PATENT ASSIGNEE(S): Ajinomoto Co., Inc., Japan
SOURCE: PCT Int. Appl., 14 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002032853	A1	20020425	WO 2001-JP9068	20011016 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 200194264	A	20020429	AU 2001-94264	20011016 <--
CA 2425533	A1	20030410	CA 2001-2425533	20011016 <--
EP 1334962	A1	20030813	EP 2001-974874	20011016 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2001014728	A	20031014	BR 2001-14728	20011016 <--
RU 2287520	C2	20061120	RU 2003-111012	20011016 <--
TW 575541	B	20040211	TW 2001-90125695	20011017 <--
IN 2003CN00536	A	20050415	IN 2003-CN536	20030411 <--
US 20040224219	A1	20041025	US 2003-418102	20030418 <--
US 7030268	B2	20060418		
US 2006155143	A1	20060713	US 2005-319177	20051228 <--

PRIORITY APPLN. INFO.: JP 2000-317603 A 20001018 <--
WO 2001-JP9068 W 20011016 <--
US 2003-418102 A1 20030418

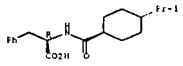
OTHER SOURCE(S): CASREACT 136:340997

AB This document discloses a process for preparing easily and simply high-purity acylphenylalanines extremely useful as raw materials of drugs or the like, characterized by reacting an acid chloride with phenylalanine in a mixed solvent consisting of an organic solvent and water under conditions made alkaline with potassium hydroxide.

IT ***105816-04-4P***
RL: ***IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)***
(process for preparation of acylphenylalanines)

RN 105816-04-4 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 19 OF 34 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:293592 HCAPLUS Full-text
DOCUMENT NUMBER: 136:325420
TITLE: Drugs for diabetes, especially type 2, comprising an antiinflammatory or analgesic drug, selected bivalent linkers, and a nitrate ester
INVENTOR(S): Del Soldato, Piero
PATENT ASSIGNEE(S): Nicox S.A., Fr.
SOURCE: PCT Int. Appl., 66 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002030867	A2	20020418	WO 2001-EP11665	20011009 <--
WO 2002030867	A3	20020725		
W: AE, AG, AL, AU, BA, BB, BG, BR, BZ, CA, CN, CR, CU, CZ, DM, DZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
IT 2000MI2201	A1	20020412	IT 2000-MI2201	20001012 <--
IT 1319201	B1	20030926		
CA 2425655	A1	20020418	CA 2001-2425655	20011009 <--
AU 2002014006	A	20020422	AU 2002-14006	20011009 <--
EP 1324974	A2	20030709	EP 2001-982414	20011009 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004511456	T	20040415	JP 2002-534256	20011009 <--
US 2004023890	A1	20040205	US 2003-398511	20030411 <--

PRIORITY APPLN. INFO.: IT 2000-MI2201 A 20001012 <--
WO 2001-EP11665 W 20011009 <--

OTHER SOURCE(S): MARPAT 136:325420
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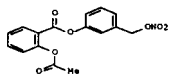


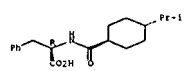
II

AB Useful for the treatment of diabetes, particularly type 2, are compds. or salts thereof, having the following general formula A-(B)n-(C)m-NO2 [I; wherein A = radical of a drug having an antiinflammatory or analgesic activity; B = bivalent linking group wherein the precursor must meet certain tests described in the application; C = another defined bivalent linking group; n and m = 0 or 1, provided that (n + m) = 1 or 2]. I can be used in conjunction with other antidiabetic drugs, particularly insulin. I increase the in vivo antidiabetic effect of insulin, and reduce complications of diabetes, particularly vascular diseases, retinopathies, neuropathies, etc.. The values of n and m, i.e., the presence or absence of bivalent linkers B and C, alone or in combination, are based on performance of the precursors of the linkers in certain tests (no data). These tests are designated as follows: (test 4A): inhibition by > 15% of hemolysis of rat erythrocytes induced by cumene hydroperoxide; (test 5): inhibition of radical production by ≥ 50% in the oxidative degradation of . desoxyribose in aqueous Fe2+(NH4)2(SO4)2/thiobarbituric acid solution; and (test 4): inhibition by ≥ 50% of DPPH-induced radical production in MeOH solution For instance, acetylsalicylic acid chloride was esterified with 3-(hydroxymethyl)phenol (80%), followed by nitation of the resultant Ph ester with HNO3/H2SO4 (82%), to give invention compound II, which is thus the 3-(nitrooxymethyl)phenyl ester of aspirin. When tested on isolated aorta from insulin-resistant rats, compound II at a concentration of 10-4 M gave 70% vasorelaxation, relative to non-insulin-resistant controls. This effect was unchanged by the presence or absence of the irreversible NO synthetase inhibitor LNNA. In contrast, both Na nitroprussiate and the indomethacin analog of II, known NO donors, were inactive, and the antidiabetic drug metformin was inactivated by LNNA.

IT ***105816-04-4DP***, Nateglinide, nitroxyl-containing derivs.
RL: PAC (Pharmacological activity); ***SPN (Synthetic preparation)***; THU (Therapeutic use); BIOL (Biological study); ***PREP (Preparation)***; USES (Uses)
(drug candidates; preparation of antidiabetic agents comprising antiinflammatory or analgesic drugs, selected bivalent linkers, and nitrate esters)

RN 105816-04-4 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (CA INDEX NAME)

Absolute stereochemistry.



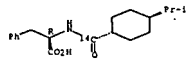
L18 ANSWER 20 OF 34 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:174779 HCAPLUS Full-text
DOCUMENT NUMBER: 137:370326
TITLE: Synthesis of [14C]- and [3H]DJN608 [STARLIX]
AUTHOR(S): Ray, T.; Ciszewska, G.; Wu, A.; Jones, L.
CORPORATE SOURCE: DMPK-Isotope Section, Novartis Pharmaceuticals, E. Hanover, NJ, USA
SOURCE: Synthesis and Applications of Isotopically Labelled Compounds, Proceedings of the International Symposium, 7th, Dresden, Germany, June 18-22, 2000 ***(2001***), , Meeting Date 2000, 228-231. Editor(s): Pleiss, Ulrich; Voges, Rolf. John Wiley & Sons Ltd.: Chichester, UK.***
CODEN: 69C1JC; ISBN: 0-471-49501-8
DOCUMENT TYPE: ***Conference***
LANGUAGE: ***English***
OTHER SOURCE(S): ***CASREACT 137:370326***

AB ***A novel oral medication for treating type 2 diabetes is trans-N-[[4-(1-methylethyl)cyclohexyl]-carbonyl]-D-phenylalanine, DJN608 [Starlix]. The key step in the synthesis of [14C]DJN608 was the catalytic redn. of [carboxy-14C]cinnic acid in the presence of PtO2 at 55 psi of hydrogen in acetic acid to give cis/trans-4-isopropylcyclohexane-[14C]carboxylic acid in 3:1 ratio. Alternatively methods for prepg. this mixt. of cis- and trans- acids (3:1) are presented. Tritiated DJN608 was prepd. by redn. of the corresponding chloro deriv. with tritium gas in the presence of 10% palladium on carbon.***

IT ***475168-21-9P***
RL: ***SPN (Synthetic preparation); PREP (Preparation)***
(stereoselective prepn. of [14C]- and [3H]DJN608 [Starlix])

RN 475168-21-9 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl-14C]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

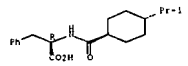


REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 21 OF 34 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:130037 HCAPLUS Full-text
DOCUMENT NUMBER: 137:325603
TITLE: Synthesis of Nateglinide
AUTHOR(S): Zhu, Xue-yan; Peng, Ka; Wang, Xiao-qin; Yang, Li-ping
CORPORATE SOURCE: Dep. Chem., East China Normal Univ., Shanghai, 200062, Peop. Rep. China
SOURCE: Hecheng Huaxue (2001), 9(6), 537-540
CODEN: HEHUEZ; ISSN: 1005-1511
PUBLISHER: Hecheng Huaxue Bianjibu
DOCUMENT TYPE: Journal

LANGUAGE: Chinese
OTHER SOURCE(S): CASREACT 137:325603
AB Title compound, a new antidiabetes medicine, was synthesized from isopropylbenzene in seven steps, giving the product with overall yield 22%.
IT ***105816-04-4DP***, Nateglinide, B crystal type
RL: RCT (Reactant); ***SPN (Synthetic preparation); PREP (Preparation)***; RACT (Reactant or reagent)
(preparation and crystalline forms of)
RN 105816-04-4 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (CA INDEX NAME)

Absolute stereochemistry.

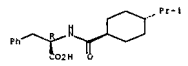


RL: ***SPN (Synthetic preparation); PREP (Preparation)***
(synthesis of Nateglinide

L18 ANSWER 22 OF 34 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:81395 HCAPLUS Full-text
DOCUMENT NUMBER: 136:256670
TITLE: Determination of nateglinide enantiomer in human plasma and urine by HPLC
AUTHOR(S): Cao, Guoying; Hu, Xin; Yan, Xiaoli; Yin, Qi; Song, Youhua
CORPORATE SOURCE: Beijing Hospital, Beijing, 100730, Peop. Rep. China
SOURCE: Yaowu Fenxi Zazhi (***2001***), 21(6), 404-407
CODEN: YFZADL; ISSN: 0254-1793
PUBLISHER: Yaowu Fenxi Zazhi Bianji Weiyuanhui
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
AB A simple method for the determination of nateglinide enantiomers in human plasma and urine was established by using HPLC on Chiralcel OD-R column (10 μm, 0.46 cm x 25 cm) with MeCN-0.5 mol L-1 NaClO4 (pH 2.2, 70:30) as mobile phase and the flow rate 0.4 mL min-1. The UV detection wavelength was 214 nm and the whole operation was under room temperature. The linearity was obtained at 0.02-20 mg L- 1 and 0.02-10 mg L-1 for D-nateglinide (r = 0.999 5 and 0.999 8) and 0.08-20 mg L-1 and 0.08-10 mg L-1 for L-nateglinide in plasma and urine, resp. The intra-day and inter-day relative standard deviation for D-nateglinide in plasma and in urine were < 6.9% and 8.2% and 7.1% and 10.0% (both n = 5), resp. The intra-day and inter-day relative standard deviation for D-nateglinidm in urine were < 7.0% and 9.8% (n = 5), resp. The intra-day and inter-day relative standard deviation for L-nateglinide in urine were < 7.2% and 10.3% (n = 5), resp. The assay was rapid and simple to allow accurate and precise measurements of D-nateglinide and its enantiomer in plasma during pharmacokinetic studies in human.
IT ***105816-04-4***, Nateglinide ***105816-05-5***
RL: ANT (Analyte); ANST (Analytical study)
(determination of nateglinide enantiomer in human plasma and urine by HPLC)
RN 105816-04-4 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (CA

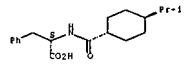
INDEX NAME)

Absolute stereochemistry.



RN 105816-05-5 HCAPLUS
CN L-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (9CI) (CA INDEX NAME)

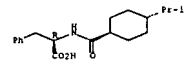
Absolute stereochemistry.



L18 ANSWER 23 OF 34 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:571834 HCAPLUS Full-text
DOCUMENT NUMBER: 136:172892
TITLE: Test for cis-isomer from N-(trans-4-isopropylcyclohexyl-carbonyl)-D-phenylalanine by RP-HPLC
AUTHOR(S): Si, Duanyun; Zhong, Dafang
CORPORATE SOURCE: Center of Instrumental Analysis, Shenyang Pharmaceutical University, Shenyang, 110016, Peop. Rep. China
SOURCE: Yaowu Fenxi Zazhi (***2001***), 21(3), 153-154
CODEN: YFZADL; ISSN: 0254-1793
PUBLISHER: Yaowu Fenxi Zazhi Bianji Weiyuanhui
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
AB A non-chiral RP-HPLC method was developed for testing of the cis-isomer from N-(trans-4-isopropylcyclohexylcarbonyl)-D- phenylalanine (I). Nucleosil C18 column was used with acetonitrile - 0.05 mol L-1 NH4H2PO4 (22.5:77.5) (pH 7.4) as mobile phase (a flow rate of 1.0 mL min-1), and 210 nm as UV detection wavelength. The electrospray ionization-quadrupole ion trap mass spectrometer was applied to verify the separation. The chromatog. peaks with a good resolution of 1.51 at 54.7 min and 49.8 min resulted from I and its cis-isomer, resp. This assay could be used as an ordinary way to test for the cis-isomer impurity of I.
IT ***105816-04-4 105816-06-6***
RL: ANT (Analyte); ANST (Analytical study)
(determination of cis-isomer from N-(trans-4-isopropylcyclohexyl-carbonyl)-D-
phenylalanine by RP-HPLC)
RN 105816-04-4 HCAPLUS

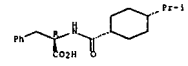
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (CA INDEX NAME)

Absolute stereochemistry.



RN 105816-06-6 HCAPLUS
CN D-Phenylalanine, N-[(cis-4-(1-methylethyl)cyclohexyl]carbonyl]- (9CI) (CA INDEX NAME)

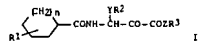
Absolute stereochemistry.



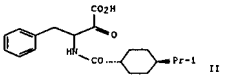
L18 ANSWER 24 OF 34 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:38482 HCAPLUS Full-text
DOCUMENT NUMBER: 134:100592
TITLE: Preparation and effect of cycloalkylcarboxamide derivatives as cysteine protease inhibitors
INVENTOR(S): Sato, Masaaki; Mukoyama, Harunobu; Kobayashi, Junichi; Tsuyuki, Shogo; Tokutake, Katsunori; Akabane, Satoshi
PATENT ASSIGNEE(S): Kissei Pharmaceutical Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 27 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2001011037	A	20010116	JP 1999-188275	19990701 <--
PRIORITY APPLN. INFO.:			JP 1999-188275	19990701 <--

OTHER SOURCE(S): MARPAT 134:100592
GI



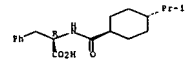
I



II

AB Title compds. {I; R1 = alkyl; Y = alkylene; R2 = OH, aryl, aryl alkoxy; R3 = H, alkyl, aryl, pyridyl, arylalkyl, pyridylalkyl; Z = O, NH; n = integer 1-3] and stereoisomers are prepared and possesses the cysteine protease inhibitory effect. Title compds. are useful in prevention of arthritis, Alzheimer's disease, rheumatism and osteoporosis. Thus, the title compound II was prepared and tested.
IT ***105816-04-4P***
RL: RCT (Reactant); ***SPN (Synthetic preparation); PREP (Preparation)***; RACT (Reactant or reagent)
(preparation and effect of cycloalkylcarboxamide derivs. as cysteine protease inhibitors)
RN 105816-04-4 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (CA INDEX NAME)

Absolute stereochemistry.



L18 ANSWER 25 OF 34 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:491334 HCAPLUS Full-text
DOCUMENT NUMBER: 133:232633
TITLE: Pancreatic β-cell KATP channel activity and membrane-binding studies with nateglinide: a comparison with sulfonylureas and repaglinide
AUTHOR(S): Hu, Shiling; Wang, Shuya; Fanelli, Barbara; Bell, Philip A.; Dunning, Beth E.; Geisse, Sabine; Schmitz, Rita; Boettcher, Brian R.
CORPORATE SOURCE: Metabolic and Cardiovascular Disease Department, Novartis Institute for Biomedical Research, Summit, NJ, USA

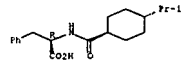
SOURCE: Journal of Pharmacology and Experimental Therapeutics (*2000*), 293(2), 444-452
CODEN: JPETAB; ISSN: 0022-3565
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Nateglinide (A-4166) is an amino acid derivative with insulinotrophic action in clin. development for treatment of type 2 diabetes. The aim of this study was to determine whether nateglinide's interaction at the KATP channel/sulfonylurea receptor underlies its more rapid onset and shorter duration of action in animal models. Binding studies were carried out with membranes prepared from RIN-m5F cells and HEK-293 cells expressing recombinant human sulfonylurea receptor 1 (SUR1). The relative order for displacement of [3H]glibenclamide in competitive binding expts. with RIN-m5F cell membranes was glibenclamide > glimepiride > repaglinide > glipizide > nateglinide > L-nateglinide > tolbutamide. The results with HEK-293/recombinant human SUR1 cells were similar with the exception that glipizide was more potent than repaglinide. Neither nateglinide nor repaglinide had any effect on the dissociation kinetics for [3H]glibenclamide, consistent with both compds. competitively binding to the glibenclamide-binding site on SUR1. Finally, the inability to measure [3H]nateglinide binding suggests that nateglinide dissocs. rapidly from SUR1. Direct interaction of nateglinide with KATP channels in rat pancreatic β-cells was investigated with the patch-clamp method. The relative potency for inhibition of the KATP channel was repaglinide > glibenclamide > nateglinide. Kinetics of the inhibitory effect on KATP current showed that the onset of inhibition by nateglinide was comparable to glibenclamide but more rapid than that of repaglinide. The time for reversal of channel inhibition by nateglinide was also faster than with glibenclamide and repaglinide. These results suggest that the unique characteristics of nateglinide are largely the result of its interaction at the KATP channel.

IT ***105816-04-4***, Nateglinide ***105816-05-5***
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(pancreatic β-cell KATP channel activity and membrane-binding studies with nateglinide and comparison with sulfonylureas and repaglinide)

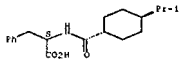
RN 105816-04-4 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (CA INDEX NAME)

Absolute stereochemistry.



RN 105816-05-5 HCAPLUS
CN L-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

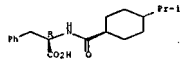
L16 ANSWER 26 OF 34 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1997:125380 HCAPLUS Full-text
DOCUMENT NUMBER: 126:195095
TITLE: General pharmacology of AY4166, a novel oral hypoglycemic agent
AUTHOR(S): Maeda, Kazutoshi; Arisaka, Harumi; Kihara, Hideaki; Sakonjo, Hiroshi; Tsuchiyama, Michio; Ikeda, Hironobu; Kimura, Ayahito; Nishimura, Takaharu; Nishimori, Tsukao; Iwata, Seinosuke; Yoshimoto, Ryoto
CORPORATE SOURCE: Life Sci. Lab., Central Res. Lab., Ajinomoto Co., Inc., Japan
SOURCE: Yakuri to Chiryo (*1997*), 25(Suppl. 1), S/157-S/180
CODEN: YACHDS; ISSN: 0386-3603
PUBLISHER: Raifu Saiensu Shuppan K.K.
DOCUMENT TYPE: Journal
LANGUAGE: Japanese

AB The general pharmacol. properties of AY4166, an oral hypoglycemic agent, were investigated in exptl. animals. In addition to AY4166, its metabolites, its Et ester, and its optical isomer were studied for their effects on gross behavior. Data are given with regard to the effects of AY4166 on the central and autonomic nervous systems, smooth muscles, respiratory, cardiovascular, digestive, and urinary systems, and blood platelet aggregation. In all these cases, the effects were absent or slight. The metabolites, the Et ester and the (+)-enantiomer had no effects on gross behavior in mice. These results suggest that AY4166 would not cause any severe side effects when given at clin. doses.

IT ***105816-04-4***, AY 4166
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(general pharmacol. of)

RN 105816-04-4 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (CA INDEX NAME)

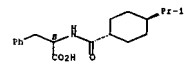
Absolute stereochemistry.



IT ***105816-05-5***
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(general pharmacol. of hypoglycemic drug AY 4166 and its enantiomer)

RN 105816-05-5 HCAPLUS
CN L-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L18 ANSWER 27 OF 34 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1995:964992 HCAPLUS Full-text
DOCUMENT NUMBER: 124:155974
TITLE: Crystals of N-(trans-4-isopropylcyclohexylcarbonyl)-D-phenylalanine and methods for preparing them
INVENTOR(S): Sumikawa, Michito; Koguchi, Yoshihito; Ohgane, Takao; Irie, Yasuo; Takahashi, Satoji
PATENT ASSIGNEE(S): Ajinomoto Co., Inc., Japan
SOURCE: U.S., 12 pp. Cont.-in-part of U.S. Ser. No. 166,144.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

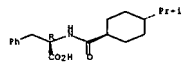
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5463116	A	19951031	US 1994-190460	19940202 <--
US 5488150	A	19960130	US 1993-166144	19931214 <--
CA 2114678	A1	19950802	CA 1994-2114678	19940201 <--
CA 2114678	C	19990427		
PRIORITY APPLN. INFO.:			JP 1991-189696 A	19910730 <--
			JP 1991-199453 A	19910808 <--
			US 1992-921224 B1	19920729 <--
			US 1993-166144 A2	19931214 <--

AB Stable crystals of N-(trans-4-isopropylcyclohexylcarbonyl)-D-phenylalanine for pharmaceutical formulation may be produced by treating this compound with a solvent at a temperature of at least 10° and forming crystals in the solvent at a temperature of at least 10°. For example, crystals may be formed by crystallization out of solution, or may be formed from solid particles of the compound suspended in a solvent. Crystals formed in this way have different m.p., IR spectrum and X-ray diffraction patterns from previously known forms of the compound and have enhanced processability, e.g., stability to grinding.

IT ***105816-04-4***
RL: PEP (Physical, engineering or chemical process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(crystallization of (isopropylcyclohexylcarbonyl)phenylalanine for enhanced stability to grinding)

RN 105816-04-4 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (CA INDEX NAME)

Absolute stereochemistry.



IT ***173653-89-9***
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(crystallization of (isopropylcyclohexylcarbonyl)phenylalanine for enhanced stability to grinding)

RN 173653-89-9 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-, hydrate (9CI) (CA INDEX NAME)

Absolute stereochemistry.

● x H_2O

L18 ANSWER 28 OF 34 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1995:68819 HCAPLUS Full-text
DOCUMENT NUMBER: 123:55430
TITLE: Preparation of trans-4-isopropylcyclohexanecarboxylic acid chloride
INVENTOR(S): Matsuzawa, Toshihiro; Irie, Yasuo
PATENT ASSIGNEE(S): Ajinomoto KK, Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 3 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 07017899	A	19950120	JP 1993-163426	19930701 <--
PRIORITY APPLN. INFO.:			JP 1993-163426	19930701 <--

OTHER SOURCE(S): CASREACT 123:55430

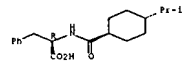
AB The title compound (I), useful as an intermediate for antidiabetic N-(trans-4-isopropylcyclohexylcarbonyl)-D-phenylalanine, is prepared by treatment of trans-4-isopropylcyclohexanecarboxylic acid (II) with P chloride. II was treated with PCl5 in 1,2-dichloroethane at 40° for 3 h to give 94% I and 0% the cis-isomer, whereas cis-isomer was detected, when SOCl2 was used instead of PCl5.

IT ***105816-04-4P***
RL: ***PNU (Preparation, unclassified); PREP (Preparation)***
(preparation of trans-4-isopropylcyclohexanecarboxylic acid chloride as intermediate for antidiabetic agent by chlorination of the acid with P chloride)

RN 105816-04-4 HCAPLUS

CN D-Phenylalanine, *N*-[(trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (CA INDEX NAME)

Absolute stereochemistry.



L18 ANSWER 29 OF 34 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1993:261002 HCAPLUS Full-text

DOCUMENT NUMBER: 118:261002

TITLE: Stable crystals of N-(trans-4-isopropylcyclohexylcarbonyl)-D-phenylalanine

INVENTOR(S): Sumikawa, Michito; Koguchi, Yoshihito; Ohgane, Takao; Irie, Yasuo; Takahashi, Satoji

PATENT ASSIGNEE(S): Ajinomoto Co., Inc., Japan

SOURCE: Eur. Pat. Appl., 14 pp.
CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 526171	A2	19930203	EP 1992-306895	19920729 <--
EP 526171	A3	19930505		
EP 526171	B1	19970305		
R: AT, CH, DE, DK, ES, FR, GB, IT, LI, LU, NL, SE				
JP 05208943	A	19930820	JP 1992-202686	19920729 <--
JP 2508949	B2	19960619		
AT 149483	T	19970315	AT 1992-306895	19920729 <--
ES 2100291	T3	19970616	ES 1992-306895	19920729 <--
CA 2114678	A1	19950802	CA 1994-2114678	19940201 <--
CA 2114678	C	19990427		
PRIORITY APPLN. INFO.:			JP 1991-189696 A	19910730 <--
			JP 1991-199453 A	19910808 <--

AB Stable H-type crystals of *N*-(trans-4-isopropylcyclohexylcarbonyl)-D-phenylalanine (I) are obtained by treating I with a solvent, at >10°. A solution of 5 g I in 20 mL acetone was added to a stirred mixture of 40 mL

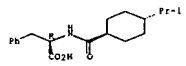
acetone and 60 mL water, at 25° to precipitate H-type crystals. The crystals have different m.p., IR spectrum and x-ray diffraction patterns from known forms of I and are not converted to other forms when ground.

IT ***105816-04-4P***
RL: ***PREP (Preparation)***
(crystals, stable, preparation of)

RN 105816-04-4 HCAPLUS

CN D-Phenylalanine, *N*-[[trans-4-(1-methylethyl]cyclohexyl]carbonyl]- (CA INDEX NAME)

Absolute stereochemistry.



L18 ANSWER 30 OF 34 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1989:464062 HCAPLUS Full-text

DOCUMENT NUMBER: 111:64062

TITLE: Separation of a new antidiabetic agent, N-(trans-4-isopropylcyclohexylcarbonyl)-D-phenylalanine, and its isomers by chiral high-performance liquid chromatography

AUTHOR(S): Shinkai, Hisashi; Nishikawa, Masahiko; Sato, Yusuke

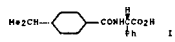
CORPORATE SOURCE: Cent. Res. lab., Ajinomoto Co., Inc., Kawasaki, 210, Japan

SOURCE: Journal of Liquid Chromatography (***1989***), 12(3), 457-64
CODEN: JLCHD8; ISSN: 0148-3919

DOCUMENT TYPE: Journal

LANGUAGE: English

GI



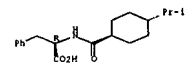
AB A4166 (I) is a new oral antidiabetic agent. To determine the purity of chemical samples of A4166, a HPLC method for the separation of A4166 and synthetic byproducts (an L-enantiomer and a cis isomer of A4166) was developed. A chiral stationary phase column packed with 5 μm *N*-(tert-butylaminocarbonyl)-L-valylaminopropyl silica gel was used for the direct separation of A4166 and its isomers after derivatization with a nonchiral reagent.

IT ***105816-04-4***, A4166
RL: ANST (Analytical study)
(separation of isomers and, by chiral HPLC)

RN 105816-04-4 HCAPLUS

CN D-Phenylalanine, *N*-[[trans-4-(1-methylethyl]cyclohexyl]carbonyl]- (CA INDEX NAME)

Absolute stereochemistry.

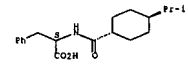


IT ***105816-05-5 105816-06-6***
RL: PROC (Process)
(separation of, as A4166 isomer, by chiral HPLC)

RN 105816-05-5 HCAPLUS

CN L-Phenylalanine, *N*-[[trans-4-(1-methylethyl]cyclohexyl]carbonyl]- (9CI) (CA INDEX NAME)

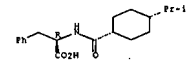
Absolute stereochemistry.



RN 105816-06-6 HCAPLUS

CN D-Phenylalanine, *N*-[[cis-4-(1-methylethyl)cyclohexyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L18 ANSWER 31 OF 34 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1989:458305 HCAPLUS Full-text

DOCUMENT NUMBER: 111:58305

TITLE: *N*-(Cyclohexylcarbonyl)-D-phenylalanines and related compounds. A new class of oral hypoglycemic agents. 2

AUTHOR(S): Shinkai, Hisashi; Nishikawa, Masahiko; Sato, Yusuke; Toi, Koji; Kumashiro, Izumi; Seto, Yoshiko; Fukuma, Mariko; Dan, Katsuaki; Toyoshima, Shigeshi

CORPORATE SOURCE: Cent. Res. Lab., Ajinomoto Co., Inc., Kawasaki, 210, Japan

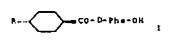
SOURCE: Journal of Medicinal Chemistry (***1989***), 32(7), 1436-41
CODEN: JMCMAR; ISSN: 0022-2623

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 111:58305

GI



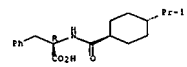
AB A series of analogs, e.g., I (R = alkyl, Ph), of *N*-(cyclohexylcarbonyl)-D-phenylalanine have been synthesized and evaluated for their hypoglycemic activity. Relationships were studied between the activity and the three-dimensional structure of the acyl moiety, which was characterized by high-resolution 1H NMR spectroscopy and MNDO calcns. The role of the carboxyl group of the phenylalanine moiety was also studied by comparing the activities of the enantiomers, the decarboxyl derivative, the esters, and the amides of the phenylalanine deriv. Thus, the structural requirements for possessing hypoglycemic activity was elucidated and a highly active compound, *N*-[(trans-4-isopropylcyclohexyl)carbonyl]-D-phenylalanine (I, R = CHMe2) was obtained, which showed a 20% blood glucose decrease at an oral dose of 1.6 mg/kg in fasted normal mice.

IT ***105816-04-4P***
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); ***EPN (Synthetic preparation)***; BIOL (Biological study); ***PREP (Preparation)***
(preparation and hypoglycemic activity of)

RN 105816-04-4 HCAPLUS

CN D-Phenylalanine, *N*-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (CA INDEX NAME)

Absolute stereochemistry.

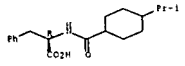


IT ***105746-37-0P***
RL: ***EPN (Synthetic preparation)***; ***PREP (Preparation)***
(preparation, amidation, hypoglycemic activity, and calculated conformation of)

RN 105746-37-0 HCAPLUS

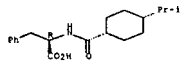
CN D-Phenylalanine, *N*-[[4-(1-methylethyl)cyclohexyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



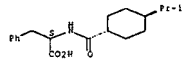
IT ***105816-06-6P***
RL: ***SPN (Synthetic preparation); PREP (Preparation)***
(preparation, hypoglycemic activity, and calculated conformation of)
RN 105816-06-6 HCAPLUS
CN D-Phenylalanine, N-[[cis-4-(1-methylethyl)cyclohexyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



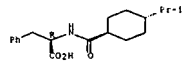
L18 ANSWER 32 OF 34 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1989:433013 HCAPLUS Full-text
DOCUMENT NUMBER: 111:33013
TITLE: Analysis of enantiomers of a new antidiabetic agent in plasma by high-performance liquid chromatography
AUTHOR(S): Sato, Yusuke; Nishikawa, Masahiko; Shinkai, Hisashi
CORPORATE SOURCE: Cent. Res. lab., Ajinomoto Co., Inc., Kawasaki, 210, Japan
SOURCE: Journal of Liquid Chromatography (*1989*), 12(3), 445-55
CODEN: JLCHD8; ISSN: 0148-3919
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A new antidiabetic agent, N-(trans-4-isopropylcyclohexylcarbonyl)-D-phenylalaone (A4166), its L-enantiomer were successfully separated and quantified by high-performance liquid chromatog. This direct resolution was accomplished using a chiral stationary phase column packed with 5 μm N-(tert-butylaminocarbonyl)-L-valylaminopropyl silica gel and mobile phase consisting of n-hexane/n-propanol/trifluoroacetic acid. The method has been used for the anal. of plasma samples from beagle dogs.
IT ***105816-05-5***
RL: ANT (Analyte); ANST (Analytical study)
(determination of, in plasma, by HPLC)
RN 105816-05-5 HCAPLUS
CN L-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT ***105816-04-4***, A4166
RL: ANT (Analyte); ANST (Analytical study)
(determination of, in plasma, by HPLC)
RN 105816-04-4 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (CA INDEX NAME)

Absolute stereochemistry.



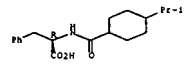
L18 ANSWER 33 OF 34 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1987:85057 HCAPLUS Full-text
Correction of: 1987:19047
DOCUMENT NUMBER: 106:85057
Correction of: 106:19047
TITLE: Preparation of D-phenylalanine derivatives and their use as hypoglycemic agents
INVENTOR(S): Toyoshima, Shigeshi; Seto, Yoshiko; Shinkai, Hisashi; Toi, Koji; Kumashiro, Izumi
PATENT ASSIGNEE(S): Ajinomoto Co., Inc., Japan
SOURCE: Eur. Pat. Appl., 25 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 196222	A2	19861001	EP 1986-302217	19860326 <--
EP 196222	A3	19880224		
EP 196222	B1	19920129		
R: CH, DE, FR, GB, LI				
JP 63054321	A	19880308	JP 1986-61833	19860319 <--
JP 04015221	B	19920317		
US 4816484	A	19890328	US 1988-146719	19880121 <--
US 34878	E	19950314	US 1993-157564	19931123 <--
			JP 1985-62276 A	19850327 <--
			JP 1986-38111 A1	19860222 <--
			US 1986-844970 A3	19860327 <--
			US 1988-146719 A5	19880121 <--

PRIORITY APPLN. INFO.:

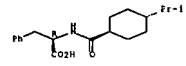
US 1989-844970 B3 19890327 <--
OTHER SOURCE(S): CASREACT 106:85057; MARPAT 106:85057
AB D-Phenylalanine derivs. D-R2CONR3CH(CO2R1)CH2Ph [I; R1 = H, C1-5 alkyl, C6-12 aryl or aralkyl, Q, CH2CO2R3, CHMeOCOR3, CH2OCOCMe3; R2 = (un)substituted C6-12 aryl, 5- or 6-membered heterocyclyl, cycloalkyl, cycloalkenyl; R3 = H, C1-5 alkyl], their salts, and precursors which can be converted thereto in the human or animal body, useful as hypoglycemics, were prepared via conventional N-acylating reactions. D-Phenylalanine in 10% aqueous NaOH was successively treated with Me2CO, 4-EtC6H4COCl in Me2CO, and 10% aqueous NaOH to give 83% acylphenylanine D-II. At 25 mg/kg in mice, D-II decreased blood glucose 34% in min.
IT ***105746-37-0P 105816-04-4P 105816-05-5P 105816-06-6P***
RL: ***SPN (Synthetic preparation); PREP (Preparation)***
(preparation of, as hypoglycemic)
RN 105746-37-0 HCAPLUS
CN D-Phenylalanine, N-[[4-(1-methylethyl)cyclohexyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



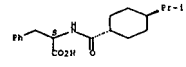
RN 105816-04-4 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (CA INDEX NAME)

Absolute stereochemistry.



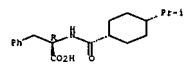
RN 105816-05-5 HCAPLUS
CN L-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 105816-06-6 HCAPLUS
CN D-Phenylalanine, N-[[cis-4-(1-methylethyl)cyclohexyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L18 ANSWER 34 OF 34 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1987:19047 HCAPLUS Full-text
DOCUMENT NUMBER: 106:19047
TITLE: Preparation of D-phenylalanine derivatives and their use as hypoglycemic agents
INVENTOR(S): Toyoshima, Shigeshi; Seto, Yoshiko; Shinkai, Hisashi; Toi, Koji; Kumashiro, Izumi
PATENT ASSIGNEE(S): Ajinomoto Co., Inc., Japan
SOURCE: Eur. Pat. Appl., 25 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 196222 A2		***19861001***EP	1986-302217	19860326
R: CH, DE, FR, GB, LI				
PRIORITY APPLN. INFO.:			JP 1985-62276	19850327

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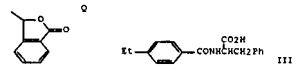
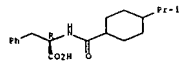


III

AB D-Phenylalanine derivs. D-R2CONR3CH(CO2R1)CH2Ph [I; R1 = H, C1-5 alkyl, C6-12 aryl or aralkyl, Q, CH2CO2R3, CHMeOCOR3, CH2OCOCMe3; R2 = (un)substituted C6-12 aryl, 5- or 6-membered heterocyclyl, cycloalkyl, cycloalkenyl; R3 = H, C1-5 alkyl], their salts, and precursors which can be converted thereto in the human or animal body, useful as hypoglycemics, were prepared via conventional N-acylating reactions. D-Phenylalanine in 10% aqueous NaOH was successively treated with Me2CO, 4-EtC6H4COCl in Me2CO, and 10% aqueous NaOH to give 83% acylphenylanine D-II. At 25 mg/kg in mice, D-II decreased blood glucose 34% in 60 min.
IT ***105746-37-0P 105816-04-4P 105816-05-5P***

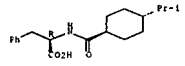
105816-06-6P
RL: ***SPN (Synthetic preparation); PREP (Preparation)***
(preparation of, as hypoglycemic)
RN 105746-17-0 HCAPLUS
CN D-Phenylalanine, N-[[4-(1-methylethyl)cyclohexyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



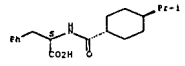
RN 105816-04-4 HCAPLUS
CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (CA INDEX NAME)

Absolute stereochemistry.



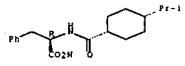
RN 105816-05-5 HCAPLUS
CN L-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 105816-06-6 HCAPLUS
CN D-Phenylalanine, N-[[cis-4-(1-methylethyl)cyclohexyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



INVENTOR NAME SEARCH

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                 ALLEN"/AU)
L20           75 SEA ("VIVILECCHIA R"/AU OR "VIVILECCHIA R V"/AU OR "VIVILECCHIA
                  RICHARD"/AU OR "VIVILECCHIA RICHARD V"/AU OR "VIVILECCHIA
                 RICHARD VICTOR"/AU)
L21         2484 SEA PARKER D/AU OR PARKER D J/AU OR PARKER D JOHN?/AU OR
                 PARKER DAVE/AU OR PARKER DAVE J?/AU OR PARKER DAVID/AU OR
                 PARKER DAVID J?/AU
L22          317 SEA DELACRUZ M/AU OR DELACRUZ MARILYN?/AU OR DELACRUZ M ?/AU
                 OR DE LA CRUZ M/AU OR DE LA CRUZ M ?/AU OR DE LA CRUZ MARILYN?/
                 AU OR DELA CRUZ M/AU OR DELA CRUZ M ?/AU OR DELA CRUZ MARILYN?/
                 AU OR DE LACRUZ M/AU OR DE LACRUZ M ?/AU OR DE LACRUZ MARILYN?/
                 AU
L23            3 SEA (L19 AND (L20 OR L21 OR L22)) OR (L20 AND (L21 OR L22)) OR
                 (L21 AND L22)
L24         3271 SEA (L19 OR L20 OR L21 OR L22)
L25            8 SEA L24 AND ?NATEGLINID?
L26            9 SEA L23 OR L25

=> dup rem 126
PROCESSING COMPLETED FOR L26
L28            5 DUP REM L26 (4 DUPLICATES REMOVED)
                 ANSWERS '1-4' FROM FILE HCAPLUS
                 ANSWER '5' FROM FILE MEDLINE

=> d l28 ibib abs tot

L28 ANSWER 1 OF 5 HCAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 1
ACCESSION NUMBER:        2006:733033 HCAPLUS Full-text
DOCUMENT NUMBER:         145:174316
TITLE:                   Direct compression formulation comprising
                         dipeptidylpeptidase IV inhibitor
INVENTOR(S):             Pfeffer, Sabine; Schaefer, Frank; Schneeberger,
                         Ricardo; Sutton, Paul Allen; Trueby, Martin
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                         Friedrich; Wirth, Wolfgang
PATENT ASSIGNEE(S):      Novartis A.-G., Switz.; Novartis Pharma G.m.b.H.
SOURCE:                  PCT Int. Appl., 100 pp.
                         CODEN: PIXXD2
DOCUMENT TYPE:           Patent
LANGUAGE:                English
FAMILY ACC. NUM. COUNT:  1
PATENT INFORMATION:

     PATENT NO.          KIND  DATE        APPLICATION NO.        DATE
     ----------------    ----  --------    --------------------   --------
     WO 2006078593        A2   20060727    WO 2006-US1473         20060117
     WO 2006078593        A3   20060914
         W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
            CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
            GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR,
            KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX,
            MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE,
            SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC,
            VN, YU, ZA, ZM, ZW
         RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
            IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,
            CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,
            GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
            KG, KZ, MD, RU, TJ, TM
     US 2006210627        A1   20060921    US 2006-333582         20060117
PRIORITY APPLN. INFO.:                     US 2005-644645P     P  20050118
                                           US 2005-690484P     P  20050614
AB   This invention relates to tablets especially tablets formed by direct
     compression of a dipeptidylpeptidase IV (DPP-IV) inhibitor compound, a process
     for the preparation thereof, to new pharmaceutical formulations, and new
     tableting powders comprising DPP-IV inhibitor formulations capable of being
     directly compressed into tablets. The invention relates further to a process
     for preparing the tablets by blending the active ingredient and specific
     excipients into the new formulations and then directly compressing the
     formulations into the direct compression tablets. The invention also relates
     to vildagliptin particle size distribution and a new crystal form of
     vildagliptin particularly adapted for the preparation of improved tablets and
     other pharmaceutical compns. For example, tablets were produced containing
     LAF237 100 mg , microcryst. cellulose 191.36 mg, lactose anhydrous 95.64 mg,
     sodium starch glycolate 8 mg and magnesium stearate 5 mg.

L28 ANSWER 2 OF 5 HCAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 3
ACCESSION NUMBER:        2003:837029 HCAPLUS Full-text
DOCUMENT NUMBER:         139:328379
TITLE:                   Crystal polymorphism of nateglinide
INVENTOR(S):             Sutton, Paul Allen
PATENT ASSIGNEE(S):      Novartis A.-G., Switz.; Novartis Pharma G.m.b.H.
SOURCE:                  PCT Int. Appl., 10 pp.
                         CODEN: PIXXD2
DOCUMENT TYPE:           Patent
LANGUAGE:                English
FAMILY ACC. NUM. COUNT:  1
PATENT INFORMATION:

     PATENT NO.          KIND  DATE        APPLICATION NO.        DATE
     ----------------    ----  --------    --------------------   --------
     WO 2003087038        A1   20031023    WO 2003-EP3664         20030414
         W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
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CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LT, LU, LV, MA, MD, MK, MN, MX, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SE, SG, SK, TJ, TM, TN, TR, TT, UA, US, UZ, VC, VN, YU, ZA, ZW
RW: AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR

CA 2482669	A1	20031023	CA 2003-2482669		20030414
AU 2003242520	A1	20031027	AU 2003-242520		20030414
EP 1497258	A1	20050119	EP 2003-746296		20030414
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK					
BR 2003009210	A	20050209	BR 2003-9210		20030414
CN 1664481	A	20050727	CN 2003-808436		20030414
JP 2005522503	T	20050728	JP 2003-583994		20030414
US 2005256336	A1	20051117	US 2004-510927		20041102
PRIORITY APPLN. INFO.:			US 2002-372625P	P	20020415
			WO 2003-EP3864	W	20030414

AB New crystal forms of N-(trans-4-isopropylcyclohexylcarbonyl)-D- phenylalanine (i.e., **nateglinide**) are produced by dissolving **nateglinide** in any of its forms, including solvates, in an organic solvent to form a solution followed by precipitation of **nateglinide** from the solution, and isolating and drying the precipitated crystal form of **nateglinide**. The precipitation of **nateglinide** may be induced either by cooling the solution, or by addition of another solvent which is miscible with the first solvent but in which **nateglinide** is only poorly soluble, or by combination of the two. Depending on the solvent a specific crystal form of **nateglinide** may be obtained, e.g., the R'-type crystal form of **nateglinide** produced by the described method has a different m.p., infra red spectra and X-ray diffraction patterns from the previously known crystal forms of **nateglinide**.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 3 OF 5 HCAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 4
ACCESSION NUMBER: 2003:737716 HCAPLUS Full-text
DOCUMENT NUMBER: 139:230996
TITLE: Preparation and properties of **nateglinide** salts
INVENTOR(S): **Sutton, Paul Allen; Vivilecchia, Richard Victor; Parker, David John; De La Cruz, Marilyn**
PATENT ASSIGNEE(S): Novartis Ag, Switz.; Novartis Pharma Gmbh
SOURCE: PCT Int. Appl., 46 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003076393	A1	20030918	WO 2003-EP2447	20030310
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LT, LU, LV, MA, MD, MK, MN, MX, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SE, SG, SK, TJ, TM, TN, TR, TT, UA, US, UZ, VC, VN, YU, ZA, ZW				
RW: AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR				

CA 2478599	A1	20030918	CA 2003-2478599		20030310
AU 2003214112	A1	20030922	AU 2003-214112		20030310
EP 1483232	A1	20041208	EP 2003-709769		20030310
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK					
BR 2003008316	A	20041228	BR 2003-8316		20030310
JP 2005519949	T	20050707	JP 2003-574615		20030310
CN 1642904	A	20050720	CN 2003-805803		20030310
US 2005234129	A1	20051020	US 2004-507255		20040928
PRIORITY APPLN. INFO.:			US 2002-363178P	P	20020311
			WO 2003-EP2447	W	20030310

AB The invention relates to salts of **nateglinide** having specified properties (m.ps., solubilities, X-ray diffraction patterns) for use in pharmaceutical compns. for preventing or treating diabetes, cardiovascular diseases, etc. **Nateglinide** Na, K, Ca, Mg, N-methyl-D-glucamine, TRIS, lysine, and ammonium salts were prepared and their properties tabulated.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 4 OF 5 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:624188 HCAPLUS Full-text
DOCUMENT NUMBER: 143:487981
TITLE: The use of thermal desorption GC/MS to study weight loss in thermogravimetric analysis of di-acid salts
AUTHOR(S): Pan, Changkang; Liu, Frances; **Sutton, Paul; Vivilecchia, Richard**
CORPORATE SOURCE: Pharmaceutical and Analytical Development, Novartis Pharmaceuticals Corporation, East Hanover, NJ, 07936, USA
SOURCE: Thermochimica Acta (2005), 435(1), 11-17
CODEN: THACAS; ISSN: 0040-6031
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Thermal desorption gas chromatograph mass spectrometry (TD GC/MS) was used to study weight loss in TGA. The technique of thermal desorption uses the same temperature heating rate as the TGA to thermally desorb volatiles from solid sample matrixes. Volatiles were cryo-trapped at -60°. After thermal desorption is complete, the trapped volatiles are separated by a GC capillary column and identified by mass spectrometry. The TD GC/MS was applied in pharmaceutical development to understand the chemical reactions attributed to the weight loss in the thermal decomposition of two dicarboxylic acid salts of a drug substance. These two salts exhibited different thermal stabilities. The thermally induced chemical reactions obtained from these two salts included dehydration and decarboxylation. Thermal degradation compds. were identified and reaction pathways for decomposition are proposed. The stability of the salts is dependent on the identity of the dicarboxylic acids from which they were generated. The information obtained from TD GC/MS helps better understand the weight loss process in TGA.

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 5 OF 5 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 2006129424 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 16426778
TITLE: Elimination of metformin-croscarmellose sodium interaction by competition.
AUTHOR: Huang W X; Desai M; Tang Q; Yang R; **Vivilecchia R V**; Joshi Y
CORPORATE SOURCE: Novartis Pharmaceutical Corporation, Pharmaceutical

Analytical Development, East Hanover, NJ 07936, USA.. wei.huang@pharma.novartis.com
SOURCE: International journal of pharmaceutics, (2006 Mar 27) Vol. 311, No. 1-2, pp. 33-9. Electronic Publication: 2006-01-19.
Journal code: 7804127. ISSN: 0378-5173.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200610
ENTRY DATE: Entered STN: 7 Mar 2006
Last Updated on STN: 17 Oct 2006
Entered Medline: 16 Oct 2006

AB During analytical method development and validation, a strong charge interaction between metformin and croscarmellose sodium was observed when the aqueous solution containing metformin was spiked with croscarmellose sodium. The charge interaction resulted in the retention of metformin in croscarmellose sodium and caused a serious drug recovery problem. The percent recovery of metformin in the solution was much lower than its theoretical values, especially in the low metformin concentration range. To overcome the metformin-croscarmellose interaction, arginine was selected as a competitor for the binding sites on croscarmellose sodium. Because of the competition and stronger interaction between arginine and croscarmellose sodium than metformin and croscarmellose sodium, a complete recovery of metformin in presence of arginine in both low and high concentration ranges was achieved. The effect of arginine on the recovery of metformin and the competition mechanism are discussed in this paper.

SEARCH HISTORY

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=> d his nofil

     (FILE 'HOME' ENTERED AT 16:17:35 ON 01 MAY 2007)

     FILE 'REGISTRY' ENTERED AT 16:17:51 ON 01 MAY 2007
                E NATEGLINIDE/CN
L1              1 SEA ABB=ON  PLU=ON  NATEGLINIDE/CN
                D

     FILE 'REGISTRY' ENTERED AT 16:18:18 ON 01 MAY 2007
L2              STR 105816-04-4
L3              2 SEA FAM SAM L2
L4             35 SEA FAM FUL L2

     FILE 'HCAPLUS' ENTERED AT 16:18:45 ON 01 MAY 2007
L5            543 SEA ABB=ON  PLU=ON  L4
                E WO2003-EP2447/APPS
L6              1 SEA ABB=ON  PLU=ON  (WO2003-EP2447/AP OR WO2003-EP2447/PRN)
                D SCA
L7             46 SEA ABB=ON  PLU=ON  L4(L)PRP/RL
                E US2002-363178P/APPS
L8              1 SEA ABB=ON  PLU=ON  US2002-363178P/PRN
L9              1 SEA ABB=ON  PLU=ON  L8 OR L6
L10           253 SEA ABB=ON  PLU=ON  L5 AND (PY<2003 OR PRY<2003 OR AY<2003)
L11            25 SEA ABB=ON  PLU=ON  L7 AND L10
L12            38 SEA ABB=ON  PLU=ON  L4(L)PREP+NT/RL

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     FILE 'HCAPLUS' ENTERED AT 16:23:02 ON 01 MAY 2007
L13             ANALYZE PLU=ON  L5 1-543 RN :   17180 TERMS
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L14             1 SEA ABB=ON  PLU=ON  105816-04-4
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L*** DEL       13 S L14 NOT L14

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     FILE 'REGISTRY' ENTERED AT 16:24:52 ON 01 MAY 2007
L15            34 SEA ABB=ON  PLU=ON  L4 NOT L14

     FILE 'HCAPLUS' ENTERED AT 16:25:12 ON 01 MAY 2007
L16            29 SEA ABB=ON  PLU=ON  L15
L17            53 SEA ABB=ON  PLU=ON  L12 OR L16
L18            34 SEA ABB=ON  PLU=ON  L17 AND L10

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L19           402 SEA ABB=ON  PLU=ON  ("SUTTON P"/AU OR "SUTTON P A"/AU OR
                "SUTTON PAUL"/AU OR "SUTTON PAUL A"/AU OR "SUTTON PAUL
                ALAN"/AU OR "SUTTON PAUL ALLEN"/AU)
                E VIVILECCHIA R/AU
L20            75 SEA ABB=ON  PLU=ON  ("VIVILECCHIA R"/AU OR "VIVILECCHIA R
                V"/AU OR "VIVILECCHIA RICHARD"/AU OR "VIVILECCHIA RICHARD
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               V"/AU OR "VIVILECCHIA RICHARD VICTOR"/AU)
L21         2484 SEA ABB=ON  PLU=ON  PARKER D/AU OR PARKER D J/AU OR PARKER D
                 JOHN?/AU OR PARKER DAVE/AU OR PARKER DAVE J?/AU OR PARKER
                 DAVID/AU OR PARKER DAVID J?/AU
                 E DELACRUZ M/AU
                 E DE LA CRUZ M/AU
L22          317 SEA ABB=ON  PLU=ON  DELACRUZ M/AU OR DELACRUZ MARILYN?/AU OR
                 DELACRUZ M ?/AU OR DE LA CRUZ M/AU OR DE LA CRUZ M ?/AU OR DE
                 LA CRUZ MARILYN?/AU OR DELA CRUZ M/AU OR DELA CRUZ M ?/AU OR
                 DELA CRUZ MARILYN?/AU OR DE LACRUZ M/AU OR DE LACRUZ M ?/AU OR
                 DE LACRUZ MARILYN?/AU
L23            3 SEA ABB=ON  PLU=ON  (L19 AND (L20 OR L21 OR L22)) OR (L20 AND
                 (L21 OR L22)) OR (L21 AND L22)
L24         3271 SEA ABB=ON  PLU=ON  (L19 OR L20 OR L21 OR L22)
L25            8 SEA ABB=ON  PLU=ON  L24 AND ?NATEGLINID?
L26            9 SEA ABB=ON  PLU=ON  L23 OR L25

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L27           33 DUP REM L18 (1 DUPLICATE REMOVED)
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               D QUE L18
               D L18 IBIB ABS HITSTR TOT

     FILE 'HCAPLUS, MEDLINE, EMBASE, BIOSIS, DISSABS, WPIX' ENTERED AT
     16:37:38 ON 01 MAY 2007
               D QUE L26
L28            5 DUP REM L26 (4 DUPLICATES REMOVED)
                    ANSWERS '1-4' FROM FILE HCAPLUS
                    ANSWER '5' FROM FILE MEDLINE
               D L28 IBIB ABS TOT
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